CIBA FOUNDATION COLLOQUIA ON AGEING

Vol. 5. The Lifespan of Animals

Leaflets giving details of available earlier volumes in this series, and also of the Ciba Foundation General Symposia, Colloquia on Endocrinology, and Study Groups, are available from the Publishers.

CIBA FOUNDATION

COLLOQUIA ON AGEING

VOLUME 5

The Lifespan of Animals

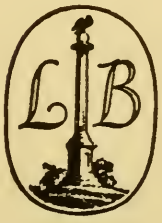
Editors for the Ciba Foundation

G. E. W. WOLSTENHOLME, *O.B.E.*, M.A., M.B., M.R.C.P.

and

MAEVE O'CONNOR, B.A.

With 58 Illustrations
and Cumulative Index to Volumes 1–5



LITTLE, BROWN AND COMPANY

BOSTON

THE Ciba Foundation, a unique international institution, owes its inception to the generosity of CIBA Limited, Basle. However, being established under British trust law, it enjoys complete independence in practice and policy.

Under the guidance of its distinguished Trustees, the Foundation offers accommodation to scientists from all over the world at its home in Portland Place. Foremost in its activities is the organization of small conferences, the proceedings of which are published in book form in the manner of the present volume. The Foundation convenes many other informal discussions between research workers of different disciplines and different nationalities and each year invites an outstanding authority to deliver a special lecture. An exchange programme between French and British postgraduates is conducted and a library service is available. Furthermore, the Ciba Foundation attempts in every other way possible to aid scientists, whether they be Nobel Laureates or young graduates making their first original contribution to research.

The purpose of the Ciba Foundation, which is to promote international co-operation in medical and chemical research, is symbolized in the armorial bearings by five interlaced rings representing the continents, a black sacrificial cock (emblem of Aesculapius) holding a medical caduceus, and three regular hexagons for chemistry. Its domicile in London is indicated by the red sword of St. Paul and the British lion; the wyvern and the crozier, symbols associated with Basle, refer to the sponsoring firm located in this ancient Swiss town.

PREFACE

EARLY in 1954 the Trustees of the Ciba Foundation designated funds over a period of five years for the encouragement of basic research relevant to the problems of Ageing. One feature of this special programme was to be the organization of small international conferences, on lines familiarly known at the Foundation in regard to other subjects in medical research, to assemble and consider such information as could be gathered in the youthful work of ageing research.

This volume contains the proceedings of the fifth Colloquium on Ageing, and also a combined index to this and the previous four volumes. The Trustees now suspend the Foundation's special stimulation of work in this field. The Director believes that considerable attention has been drawn to the many large gaps in knowledge which must be filled before the postponement and amelioration of senescence can be realized. Research workers should now be left to their task, the size and importance of which cannot be exaggerated. When exciting progress has been made, the Director will, no doubt, be anxious to arrange for further conferences and discussions as part of the general programme of the Foundation.

The Director and his co-Editor wish to place on record with these proceedings the indebtedness of the Foundation and themselves to Professor Danielli and Dr. Comfort for giving life to this meeting; to Dr. Genese and Miss Chater for its administration; to Mr. William Hill for his skill and speed in indexing; and to Messrs. J. & A. Churchill Ltd. and Messrs. Spottiswoode, Ballantyne & Co. Ltd. for minimizing, without skimping or harassment, the delay in publication in this difficult year.

CONTENTS

List of those participating in or attending the Colloquium on "The Lifespan of Animals", 14th-16th April, 1959

B. Benjamin	Dept. of Statistics, General Register Office, London
B. N. Berg	Dept. of Pathology, Columbia University College of Physicians and Surgeons, New York
R. J. H. Beverton	Min. of Agriculture, Fisheries and Food, Fisheries Laboratory, Lowestoft, Suffolk
F. Bourlière	Dept. of Physiology, Faculté de Médecine, Paris
D. H. Chitty	Bureau of Animal Population, University Oxford
A. Comfort	Dept. of Zoology, University College London
J. F. Danielli	Dept. of Zoology, King's College, London
S. D. Gerking	Dept. of Zoology, Indiana University, Bloomington, Indiana
H. Grüneberg	Medical Research Council Group for Experimental Research in Inherited Diseases, University College, London
W. Hartwig	Stade Herdbuchgesellschaft, Stade, Germany
H. E. Hinton	Dept. of Zoology, University of Bristol
S. J. Holt	Research Programmes Section, Fisheries Biology Branch, F.A.O.U.N., Rome
Eeva Jalavisto	Inst. of Physiology, Helsinki
W. E. Kershaw	Dept. of Parasitology and Entomology, University of Liverpool
Patricia J. Lindop	Dept. of Physiology, St. Bartholomew's Hospital Medical College, London
Anna Maurizio	Bienenabteilung, Eidg. Milchwirtschaftliche Versuchsanstalt, Liebefeld-Bern
O. Mühlbock	Netherlands Cancer Inst., Amsterdam
R. F. Nigrelli	New York Aquarium, New York
W. Perks	Pearl Assurance Co. Ltd., London
M. Rockstein	Dept. of Physiology, Bellevue Medical Center, New York University
J. Rotblat	Dept. of Physics, St. Bartholomew's Hospital Medical College, London

G. A. Sacher . . .	Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Illinois
S. Scheidegger . . .	Inst. of Pathology, University of Basle
J. Maynard Smith . .	Dept. of Zoology, University College London
J. M. Tanner . . .	Inst. of Child Health, Hospital for Sick Children, London
F. Verzár . . .	Gerontology Laboratory, Inst. of Anatomy, University of Basle
V. B. Wigglesworth .	Dept. of Zoology, University of Cambridge

CHAIRMAN'S OPENING REMARKS

J. F. Danielli

The investigation of problems of ageing is still in its early stages. One major reason for this is that observations must be made on old animals, which are not readily come by. A research worker in this field must have patience above average, or he will not wait until his animals are sufficiently old. And he must have money above average, or he will not be able to afford to keep his animals sufficiently long. Even where patience is available, the money is usually not.

In view of this, we must remember that, where data presented in this colloquium seem inadequate, it is usually the cost of getting better information which is the main restricting factor.

This colloquium arose largely as a result of the enthusiasm and initiative of Alex Comfort, and despite the seeming paucity of data the contributors appear to have succeeded in producing a fascinating group of papers.

ACTUARIAL ASPECTS OF HUMAN LIFESPANS

B. Benjamin
General Register Office, London

Actuaries have always been profoundly interested in the variation in the incidence of mortality with age since many of their calculations of contingencies depend upon this variation. The study of this age variation in mortality has given rise to a number of hypothetical "laws" of mortality based on theories about the exertion on the human body of deleterious influences or about the wearing out of components of the body and the exhaustion of living resources. These theories date from Gompertz (1825) who argued on physiological grounds that the intensity of mortality (in his terms the average exhaustion of man's power to avoid death) gained equal proportions in equal intervals of age and Makeham (1867) who introduced a constant component as well as a logarithmically increasing component of the force* of mortality as a reflection

* It is necessary to define certain functions of the life-table:

(1) l_x, the number still living at exact age out of an original generation of l_0 births (l_0 is called the radix of the table).

(2) d_x, the number dying between exact ages x and $x + 1$ $(= l_x - l_{x+1})$

(3) p_x, the chance of surviving from exact age x to exact $x + 1$

$$\left(= \frac{l_{x+1}}{l_x}\right)$$

(4) q_x, the chance of dying between exact age x and exact $x + 1$

$$\left(= \frac{d_x}{l_x}\right)$$

Note: $p_x + q_x = 1$

(5) μ_x, the force of mortality. The concept is of an "instantaneous" rate. It is approached by expressing the average rate of mortality at age x (m_x) over a finite interval of time as the ratio of (deaths at age x in the interval) to (average population at age x in the interval)

of the division of causes of death into two kinds, those due to chance and those due to deterioration.

It was soon evident that such a relatively simple law would not represent mortality experience throughout life and subsequent developments led to the proposal of more complex mathematical relationships between age and the force of mortality and even of different relationships over different parts of the age range. Thiele (1871) for example proposed

$$\mu_x = a_1\, e^{-b_1 x} + a_2\, e^{-b_2^2 (x-c)^2} + a_3\, e^{b_3 x}$$

in which the last term is a Gompertz curve to represent old-age mortality, the first a decreasing Gompertz curve to represent the mortality in childhood, and the middle term a normal curve. Perks (1932) introduced a new family of curves in the general form

$$\mu_x = \frac{A + Bc^x}{Kc^{-x} + 1 + Dc^x}$$

and rationalized this procedure with some interesting speculations on the theory of mortality. He found an analogy between the "inability to withstand destruction" of Gompertz and the then current physical concept of entropy change —the measure of the time progression of a statistical group from organization to disorganization. Perks also referred to the previous work of Karl Pearson who fitted overlapping curves not to the force of mortality but to the curve of deaths, the curves being intended to represent the mortality of old age, middle life, youth, childhood, and infancy, the causes of death being different in these different periods of life. Perks pointed out that this search for homogeneity in the pattern of causes of death might lead to endless subdivision

and then considering what happens to m_x when the interval of time becomes infinitely small. Clearly then the deaths between ages x_1 and x_2 in the life-table $= \int_{x_1}^{x_2} \mu_x.l_x.dx.$ and $d_x = \int_{x}^{x+1} \mu_x.l_x.dx.$

The continuous curve of $(\mu_x.l_x)$ is called the curve of deaths.

of the curve of deaths into component curves and that it was questionable whether such subdivision could be theoretically validated. Nevertheless he agreed that one important case of sudden change of composition was the rapid transition between the period of physical growth and the adult period. "In the adult period we appear to be subject to a continually increasing disorganisation or 'inability to withstand destruction' while in childhood we appear on balance to gain organisation or 'ability to withstand destruction'."

While further work continued on the fitting of mathematical functions to the force of mortality, μ_x, attention was focused on the curve of deaths (i.e. of $\mu_x.l_x$) as an alternative operand by a paper by Phillips (1935), though this was not yet to be taken up. Meanwhile, taking a closer look at the concept of deterioration, Rich (1940) evolved a theory of mortality based on an analogy between degrees of health and degrees of temperature. This gave rise to a "health frequency distribution" (a concept close to the present view of biological normality as a dispersion of characteristics within broadly separated limits), and changes of rating within this distribution could be regarded as forces of deterioration or of recuperation. A "natural law of mortality" emerged from which Makeham's and one of Perks's functions could be derived as special cases.

Clarke (1950) took up again the analysis of the curve of deaths. He argued that mortality improvements had not extended the natural lifespan but had only allowed more to achieve it. He distinguished between "anticipated" and "senescent" deaths; the ages at death in the latter group were measures of natural lifespans and had a frequency distribution like other animal characteristics. His paper formed the basis of the present work and his hypothesis will be referred to again presently.

Beard (1950) also paid attention to the curve of deaths, using the incomplete gamma function as the basic analytical function.

Later, in a discussion of another paper on fitting a mathematical law to l_x of the mortality table (Ogborn, 1953), Perks suggested that reference to the probability models of the biological field and the data of simple populations was the only way in which an advance would be made in the development of a satisfactory theory of a life-table. It is a pity that this suggestion has not yet been exploited as, if linked with the idea of loss of biological organization, it seems to the present author to open up an important line of approach. But we are straying from the objective of this historical introduction.

In 1954 Phillips returned to consideration of the curve of deaths and hypothesized the existence of a basic curve of deaths "to which all curves of deaths are, as it were, striving to attain".

Clarke's division of deaths into "anticipated" and "senescent" has been further developed by Barnett (1955 and 1958) but applied to the force of mortality, not the curve of deaths. On the basis of cause of death grouping and the actual shape of the curve of observed age rates of mortality Barnett distinguished several different groups of anticipated deaths.

We may now return to Clarke's paper.

The earlier approach

The objective of Clarke's approach was the forecasting of the rates of mortality which would operate in the future. His hypothesis was that every individual carried with him from birth a genetically endowed term of life beyond which it was impossible for him to survive, and that if we knew these terms for every member of the population we could form a frequency distribution similar to that of any other biometric quantity. This distribution would represent a limiting form of the curve of deaths. Clarke went further and supposed that this distribution would not shift as a whole toward later

ages, i.e. that the modal span of life was invariant; he rejected the possibility as "intangible speculation" outside the practical framework of his study, namely the relatively short-term trend of mortality. Deaths were then divided into two categories, namely those which happened because the term of the lifespan had run out—senescent deaths—, and all others, whether from accident or disease, which were in fact a cutting short of the lifespan—anticipated deaths. He first obtained, therefore, a limiting curve of deaths by constructing a table of mortality in which the q_x (probability of death between age x and age $x + 1$) column would consist of values (q_x^s) appropriate only to causes of death which could be regarded as senescent. The next stage was to predict the pace at which actual rates of mortality would in a given future period approach those of the limiting table. It is not necessary to discuss this aspect here.

Clarke originally intended to define "senescent" deaths by choosing certain degenerative diseases (e.g. cerebral vascular lesions, myocardial diseases, angina pectoris, arteriosclerosis, other diseases of the circulatory system, bronchitis, nephritis), but he naturally found it difficult to select disease groups with sufficiently specific reference to degeneration. Ultimately therefore he arbitrarily assumed ratios of q_x^s/q_x rising from 0·05 at age 20 to 0·10 at age 40, 0·20 at age 50, 0·70 at age 70, 1·00 at ages 80 and above.

His limiting curve of deaths was not symmetrical. There was a sharp peak at age 80 with a tailing off rapidly on one side to age 100 or so and on the other side a rapid decline to about age 60 and then a much slower tailing off to age 20.

The present approach

The present author's approach has been even more arbitrary and pragmatic. In a particular life-table the values of d_x (deaths between age x and $x + 1$) have been plotted for every value of x in the table (Figs. 1–3), thus producing an

approximation to the curve of deaths (d_x is of course discontinuous while the "curve of deaths" is continuous. It has been assumed that $d_x \doteqdot \mu_{x+\frac{1}{2}}.l_{x+\frac{1}{2}}$). The curve has then been treated from its later mode (e.g. the peak at age 76 in Fig. 3) to the upper limit of age as the right-hand side of the distribution of "senescent" deaths, i.e. of normal lifespans, and the left-hand

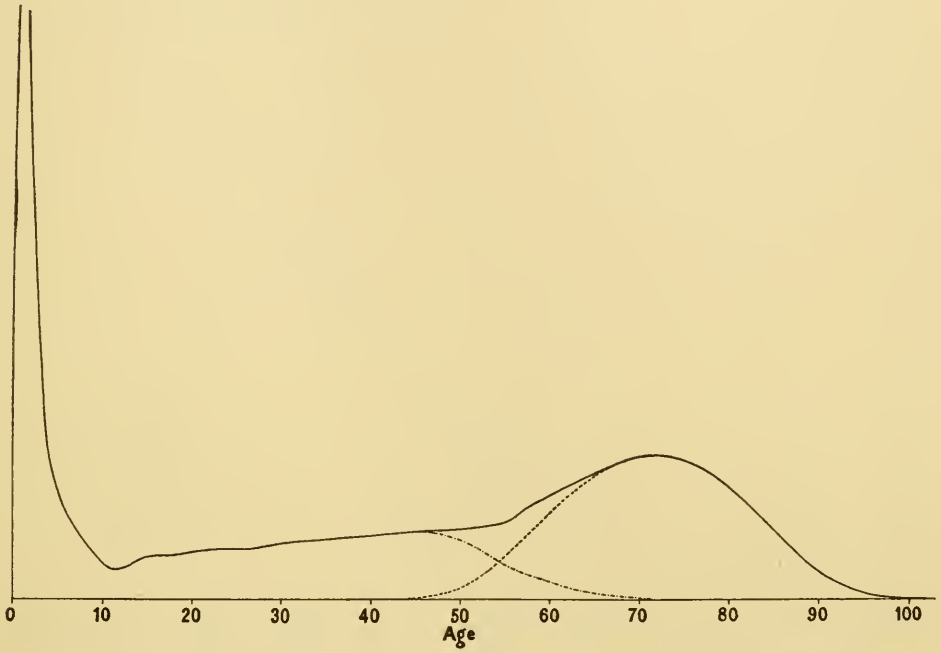


FIG. 1. Curve of deaths. English Life-Table No. 1. 1841. Males.

——————— total deaths
. . . . . senescent deaths
— . — . — . — . — . — . anticipated deaths

side of this distribution has been drawn in (broken line in the figures) to exactly mirror the right-hand side. It is thus assumed (unlike Clarke) that the biometric distribution of lifespans is symmetrical. When the deaths of this left-hand side of the distribution are subtracted from the main curve of deaths the residual (of "anticipated" deaths) tails off (by a broken line in Fig. 3) to zero at the peak of the senescent deaths. In effect it is assumed in Fig. 3 that no deaths before

age 55 and all deaths after age 76 are senescent. It is hoped that this brash sweeping aside of the honest testimonies of millions of medical practitioners which are recorded in the vaults of Somerset House will not give offence. It is of course a moot point as to whether any death after age 76, even

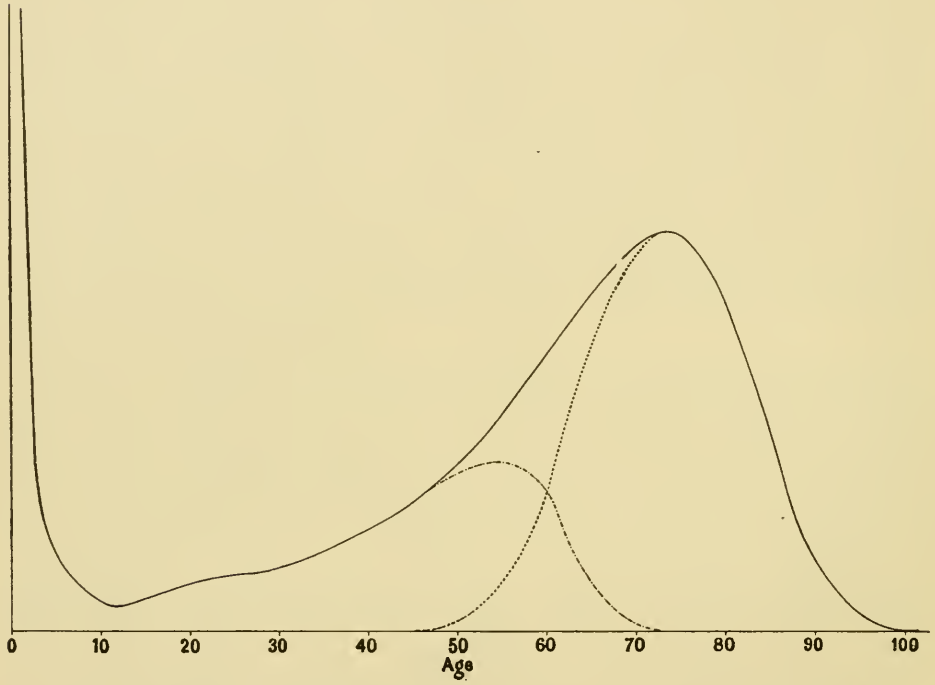


Fig. 2. Curve of deaths. English Life-Table No. 8. 1910–1912. Males.

——————— total deaths
. . . . . senescent deaths
— · — · — · — · — · — · — anticipated deaths

allegedly due to some accident, is other than of senile origin, but some deaths before age 55 are of degenerative origin and at age 55 Clarke assumed that 20 per cent of them were "senescent". Whether this degeneration is senescent in the sense of the completion of a genetically endowed lifespan or whether it is the cutting short of the span by departure from optimum environmental conditions and behaviour is at least

arguable and it is proposed to adopt the latter hypothesis here.

The data used

The analysis already described was applied to three national life-tables (for both males and females, though Figs. 1–3 relate to males only):

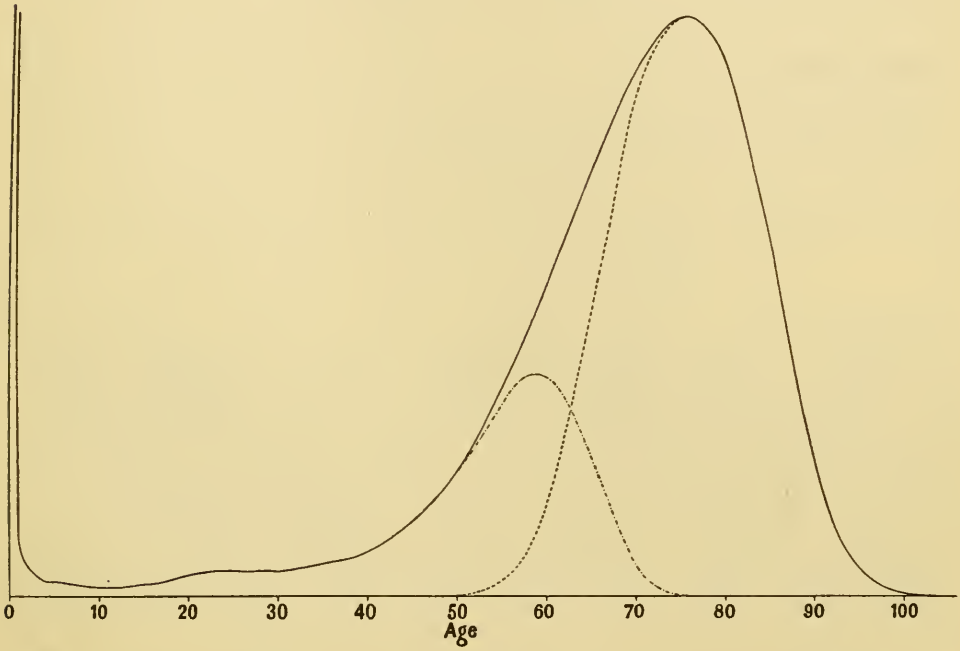


FIG. 3. Curve of deaths. English Life-Table No. 11. 1950–1952. Males.

——————— total deaths
..... senescent deaths
— . — . — . — . — . — . anticipated deaths

English Life-Table No. 1. The first to be compiled by Dr. William Farr and based on the deaths of 1841. It differs from the other two tables which in the case of both males and females start with a radix of 100,000 births, in that Farr to facilitate the product of a "persons" table chose radices of 51,274 male births and 48,726 female births (the proportions

of males and females in the births of that period). All the ordinates of Fig. 1 should therefore be almost doubled to render it comparable with Figs. 2 and 3, though the general shape is correct.

English Life-Table No. 8. The first short period table prepared by an actuary, George King, for the Registrar-General and based on the deaths of 1910–12.

English Life-Table No. 11. Based on the deaths of 1950–52 and prepared by the Government Actuary.

The results

The basic results of this analysis are:

Senescent deaths

Period of deaths	*Males*			*Females*		
	Peak age	*Standard deviation of distribution*	*Proportion of total deaths*	*Peak age*	*Standard deviation of distribution*	*Proportion of total deaths*
	years	years	%	years	years	%
1841	72·0	9·38	39·9	73·5	9·19	41·0
1910–12	73·5	8·70	51·5	76·0	8·51	55·3
1950–52	75·7	7·89	69·4	80·3	7·12	70·3

It is clear that from a practical point of view Clarke was right. The main change in the hundred years or so has been the increase in the proportion of people attaining their allotted term of lifespan, from about 40 per cent to 70 per cent, while the shift in the peak has been a mere three or four years for men and seven years for women. Judged by the standard deviation the spread of the distribution has narrowed a little but this is not a substantial change. If—and it is a large question mark—this arbitrary distribution of "senescent" deaths can be used as an indicator of the natural

distribution of lifespan in humans then it appears possible that over and above the large increase in ability to attain the allotted span, the modal span itself is slowly increasing. Even in 1841 there had been a "break through" of the barrier of three score and ten. Women can now talk modestly of "four scores".

Comparison between men and women

If the proportion of all deaths which are senescent can be used as a measure of ability to survive the allotted term of life, then the improvement in the mortality of women as compared with that of men appears more as a greater shift in the optimum than as a greater improvement in attainment. The advantage of women over men (or conversely the disadvantage of men as compared with women) is thus a very general one and calls for intense examination.

Other aspects for examination

It would be possible to forecast mortality not only by examining the medical and environmental possibilities for the reduction of anticipated deaths as Clarke suggested but also by predicting the further change in the parameters shown in the table. It is tempting for example to suggest that the national life-table in 1970–72 will show for men a modal span of almost 77 and an attainment of natural senescence by 78 per cent, but this kind of temptation will be pursued elsewhere.

Another possibility is that the "attainment" proportion (i.e. ratio of senescent deaths to all deaths) might be used as a mortality index for international comparison. This also is outside the present discussion.

The limitations of the life-table

The life-table as normally computed is based on the rates of mortality experienced by the population of all ages as they

pass through those ages within a short period of term. The population observed is therefore a combination of a large number of generations born over a very long period, as long indeed as the extent of the table. It does not follow that those who passed through age 40 in 1950–52 will experience at 60 (in 1970–72) the mortality rates given at age 60 by English Life-Table No. 11.

For actuaries the Life-Table is an experience which they know will never be reproduced but is nevertheless a model which serves to guide estimation of the future expectations.

It should therefore be borne in mind that the senescent deaths are of people born long before those whose deaths fall in the "anticipated" category, so that it is not strictly correct to compute the ratio which one group bears to the other as in the "attainment" proportions referred to above. Similarly the peak age of senescent deaths refers to generations born 70 years or so ago and does not indicate the natural lifespan of those who are now in their infancy. However, the indications of secular trend are acceptable.

Strictly we should calculate "generation life-tables", i.e. tables each based on the observed mortality of a single generation of births (for practical purposes those born in a narrow interval of years, say five) but the recorded mortality of this country does not permit the calculation of complete tables for generations separated by more than ten to 20 years.

Accuracy of age at death

In all the kinds of analysis of death rates or of the curve of deaths which are undertaken by actuaries and have been considered above, use is made of a life-table model rather than the actual deaths of a particular year in order to base the analysis on a population with a fixed birth entry, thereby avoiding the irregularities in the run of deaths from one age to another which affect the published deaths statistics of any one period and arise from birth fluctuations or other

population disturbances. It is sometimes thought that the life-table may be inaccurate at very advanced ages because of errors in the stated age of the population and deaths involved. In order to settle this issue a check was made of the ages of alleged centenarians. The Home Office supplied a list of persons (males and spinsters) reaching the age of 100 years to whom a message of congratulation had been sent from Buckingham Palace between April 1956 and June 1958 (married women were excluded because a maiden name would be needed for checking the age and would not be known). This group is somewhat selected but their age accuracy is probably not seriously affected. For the 114 persons (53 males, 61 females) on the list, my colleagues at Somerset House searched the birth registers for the relevant entries of a 100 years or so earlier (no small undertaking). Of these seven could not be found and identification was doubtful in four other cases. This left 103 identified and of these there were 92 cases where the birth entry agreed exactly with the alleged date of birth while 11 showed errors as follows:

1 day younger than stated	4
1 day older ,, ,,	2
2 days older ,, ,,	1
2 years older ,, ,,	2
5 years older ,, ,,	2
	11

Serious errors amounted therefore to only 4 per cent of the total. If anything these figures suggest a slight understatement of lifespan.

Discussion

For the purpose of indicating the tendency for natural lifespans to become longer, or for there to be a more general

approach to some as yet unknown natural lifespan (and it is difficult to separate the two concepts) the present over-simplified analysis may serve well enough. It is indeed arguable whether the present knowledge of ageing processes justifies a more recondite approach.

We may, however, discern the possible lines of future development. If it be accepted that ageing is a process of disorganization—the introduction of the random element—then we may apply, as Perks has suggested (1932), stochastic processes to study first the distribution of ages at which organization gives place to disorganization and, second, the distribution of subsequent lengths of life of the group of lives, which at each age are subject to progressive disorganization. A prerequisite is co-operative study by biologists and statisticians of available evidence of the age incidence of the discontinuity between organization and disorganization in animals. This means shifting attention from death to early signs of degeneration in healthy lives under continuous observation.

Summary

In the past hundred years or so the peak in the age distribution of deaths in the general population has moved to a more advanced age (for men from 72 to 76 years, and for women from 73 to 80), and the proportion of deaths which, on simple assumptions, might be regarded as "senescent" (i.e. of those who attain a predetermined lifespan) has increased (for both sexes from about 40 per cent to about 70 per cent). Previous analysis of the so-called "curve of deaths" is reviewed and some suggestions are made for future analysis.

REFERENCES

Barnett, H. A. R. (1955). *J. Inst. Actu.*, **81**, 105.
Barnett, H. A. R. (1958). *J. Inst. Actu.*, **84**, 212.
Beard, R. E. (1950). *Proc. Centen. Assembl. Inst. Actu.*, **2**, 12.
Clarke, R. D. (1950). *Proc. Centen. Assembl. Inst. Actu.*, **2**, 12.

GOMPERTZ, B. (1825). *Phil. Trans.*, **115**, 513.
MAKEHAM, W. M. (1867). *J. Inst. Actu.*, **13**, 325.
OGBORN, M. E. (1953). *J. Inst. Actu.*, **79**, 170.
PEARSON, K. Karl Pearson's Early Statistical Papers. Cambridge University Press (1948).
PERKS, W. (1932). *J. Inst. Actu.*, **63**, 12.
PHILLIPS, E. W. (1935). *J. Inst. Actu.*, **66**, 17.
PHILLIPS, E. W. (1954). *J. Inst. Actu.*, **80**, 289.
RICH, C. O. (1940). *J. Inst. Actu.*, **70**, 314.
THIELE, T. N. (1871). *J. Inst. Actu.*, **16**, 313.

DISCUSSION

Danielli: What is the basic mechanism underlying this shift of the death curve to the right—that is to say, why was there an improvement in mortality?

Benjamin: I cannot hazard a guess. All I could deal with was the observed deaths, and it is a fact that the peak has shifted to the right. This might be because, as Phillips has suggested, successive generations are tending to attain a sort of ideal curve of deaths—that is, a very sharp peak, even further over to the right than has yet been observed. Or it may simply be that more people are in fact surviving to a constant natural lifespan, which means that the curve, instead of being pulled to the left by what Clarke called anticipated deaths, is allowed to grow up more on the right-hand side.

Rockstein: Does the initial portion of your curve correspond closely with that for data in other countries ? There seems to be a rather high mortality rate for males in Britain during the early years.

Benjamin: I have not yet made much comparison with the life-tables of other countries. I should not have thought it was unusual for the Western countries, at least for Western Europe.

Rotblat: The peak for the anticipated deaths seems to become sharper in the 1950–52 curve. Why should this happen ? I would have expected this peak to become flatter and spread over the whole span of life, rather than sharper. If you used a skewed distribution rather than a symmetrical one perhaps you would not get this sharp peak.

Benjamin: I am very grateful that you have made that point because this sharpening of the peak in the anticipated deaths is in fact phoney; it is simply an accident of the simplified type of analysis and has no meaning so far as I can see. One can do as Clarke did: make an arbitrary assumption about the proportion of deaths which are senescent and so avoid this assumption of a symmetrical distribution. But my difficulty is that I do not know where

to draw this line. At the end of this meeting I may know a little bit more about where it should go.

Jalavisto: One should perhaps think about three curves—one independent of age, running horizontally, a second one beginning at middle age and rising with advancing age as a result of inadequate living habits, and a third one representing the random distribution of species-specific lifespan.

Have you studied the difference between the mortality curves for males and females ? In your symmetrical component curve I would expect the base to be narrower for the females. In the female and male mortality rates the Gompertz rule holds fairly well for males but in the females the assumption of a random distribution around the age of 75 years would fit the facts better.

Benjamin: The width of the symmetrical distribution for women is only slightly narrower than that for men. You would like to take a slice off the bottom right across ?

Jalavisto: Yes, but furthermore there would be one group which is quite clearly a result of externally induced pathological changes, i.e. through accumulation during decades of carcinogenic substances, of cholesterol deposits following high fat diet, slowly developing deficiency diseases, etc. Of course, they tend to increase the mortality with advancing age because they are just a function of the chronological age. These three groups, as far as I can see, can result in any form of mortality curve according to their mutual relationships. But in any case the end-point as part of a normal distribution curve comes out very clearly, I think.

Berg: There is no difference in the nature of the diseases that cause death at age 50 and those that cause death at age 80. The diseases of senescence also occur at age 50. In animals, as well as in man, the so-called diseases of senescence occur in early life.

Benjamin: That is precisely what I want to learn.

Maynard Smith: The anticipatory deaths you mentioned were presumably deaths due to causes which would kill a person at any age, and not merely if they were old. What worries me is that, whatever those causes are, it is assumed in your analysis that nobody dies from them after the ages of about 60 to 70. If there are causes which will kill people at any age they presumably will kill old people. If you allowed for the fact that old people are dying from accidental causes, as well as young people, there might be no increase in the modal age at death in the later life-tables. In other words if you continued the anticipatory death curve throughout the whole period of life, the peak might stay at about 70 to 72 instead of shifting to the right.

Benjamin: Two different kinds of error may be introduced by this over-simplified analysis. I am more worried about my first assumption that no one under the age of 55 can die of senescence. I am not so much worried about this second assumption that no one over the age of 76 can die otherwise than by senescence, because if an old person dies of an accident, it is very difficult to know whether they would have had the accident if they had not been old. In other words, although a death appears as accidental in the statistics it may still be a death of senile origin.

Danielli: To what extent can you correct your curves for accidents ? There must be some proportion of accidents occurring to which the person who was killed makes no contribution; for example there are people who get killed in railway accidents, and as passengers in cars. Then there are other accidents, such as those to car drivers and motor cyclists, to which the individual concerned does make a contribution. These two groups may show some variation with age so that the non-contributory accident, so to speak, would be more independent of age.

Benjamin: You could calculate the deaths which are due to accidents to which the individual may have made no contribution so far as these are shown by the certified causes of death. You would of course get rid of some part of that peak of "anticipated" deaths.

Comfort: In the curve for deaths of pedestrians in road accidents by age the mode is a very close fit with the curve of general deaths if allowances are made for the different risks to infants. Pedestrian deaths are an excellent measure of general vigour—the power to see a vehicle coming, jump fast enough to avoid it, and recover if it hits you (see Comfort, A. (1957). *Ciba Found. Coll. Ageing*, **3**, 7. London: Churchill).

Benjamin: Isn't it true to say that pedestrians do make a contribution to the accident ?

Comfort: They make a large contribution and that is the point. An inestimable amount of this pedestrian mortality is of an age-distributed, or age-conditioned kind. The same point arises over my horses, when I have to decide which I am going to call natural deaths and which I am going to call non-natural deaths. It is a point where the scoring convention becomes very difficult to determine.

Jalavisto: Death from appendicitis might almost be described as an accident. Mortality in appendicitis was formerly a nearly horizontal line, especially in males, and it did not rise much with age. Later on when conditions improved, it can be seen that it is especially young people who escape death from appendicitis. The result is that the curve rises and begins to resemble the form of the

usual curves of mortality seen in nearly any disease. Obviously therefore, even in these age-independent causes of death, the aged do not profit from improved conditions.

Sacher: Your analysis of the curve of deaths into three components, Dr. Benjamin, implies the hypothesis that the population is divided into three mutually exclusive sub-groups, each of which is subject to just one of the three modes of death. An alternative hypothesis is that each individual in the population is subject to all three risks. On this basis one should consider, for each individual at each age, the joint probability of dying of these diseases. The basic actuarial function for the discussion of mortality on this probability model is therefore the rate of mortality function rather than the curve of deaths, for in this model it is the contingent probabilities, the mortality rates, that combine additively. The multiple risk model seems to me to conform better to our intuitive judgments about the nature of the mortality process. The same data that you analysed in terms of the rate of the curve of deaths can be analysed in terms of the rate of mortality function. The conclusion reached is that one component, identifiable with mortality from infectious disease, has decreased markedly, whereas the component identifiable with mortality from degenerative disease (your senescent mortality) has changed very little. The changes in mortality over a period of a century were assignable primarily to the progressive change in numerical value of two parameters (Sacher, unpublished).

Gerking: What did you really mean by saying theoretical life-tables are never actually reproduced, Dr. Benjamin ?

Benjamin: A life-table is made up of a large number of generations, and people who are dying at the older ages have been born a long while earlier, so that it is only a model. You could construct a generation life-table in which you had only the mortality appropriate to people born at one particular time, but of course it would take a long while to accumulate this data because you would need to follow a generation right through. So the life-table, which is based on a short period of observation, is actually never reproduced because the environmental conditions are changing all the time. The actuary in normal practice merely uses the life-table as a model to indicate the variation of mortality from age to age, to obtain a basis for his calculations; he makes no claim that it will be reproduced in the future.

I agree with Sacher that you would have to use rates if you were applying probabilistic theory because that is more fundamental, but it did seem to me to be easier to look at this from the point of view of lifespans by stretching out the curve of deaths. If you did

what I suggested that you should do here and took a look at the application of probability theory to people who, as it were, made the change from organization to disorganization, when degeneration begins, you would have to revert to operation on the force of mortality.

Danielli: It has been alleged that people exposed to increased radiation have a decreased expectation of life. What would happen to the right-hand peak in your death curves with this particular group ?

Benjamin: I don't think there is sufficient evidence yet.

Rotblat: The general population has had such a small increase in radiation compared with natural background radiation that one would not expect to see any effect on the death curves. On the other hand we should consider various theories of ageing, for example the recent theory of Szilard, who suggests that we all start with a certain load of faults, or mutants as he calls them, and that these determine the lifespan of a population. If we accept the fact that radiations cause mutations which may influence the lifespan, then one might have expected that in the course of time there would be an increase of these faults within us, because we accumulate the radiation from generation to generation. I would expect, therefore, that the whole curve would gradually shift to the left rather than to the right.

Prof. Grüneberg, is there an equilibrium which we may expect to reach and which would take care of this ? How would such an equilibrium be affected by the fact that nowadays people who formerly would have died younger, now live longer because of conditions in a welfare state ?

Grüneberg: I think the effects of radiation fall into two categories. We may expect the ultimate appearance of more or less deleterious mutations in the homozygous condition; however, as close inbreeding is restricted in man, the appearance of recessive mutations in homozygous condition will take a long time. On the other hand, right from the beginning, we may experience the effect of these same mutations in heterozygous condition. It is now becoming increasingly clear that at least some of these mutations in heterozygous condition can be advantageous even if they are disadvantageous in homozygous condition. One might thus expect an advantageous result in the early stages of radiation when we are mainly concerned with heterozygotes; this would ultimately be counteracted by disadvantageous effects when the mutations become homozygous. It is between these opposite effects that equilibrium is likely to establish itself in the end.

Rotblat: What are the advantageous effects which one may expect from radiation in heterozygous conditions ?

Grüneberg: It appears that these are improvements of general viability. In *Drosophila* the chronic irradiation experiments of Bruce Wallace (1957. *Proc. nat. Acad. Sci.* (*Wash.*), **43**, 404) indicate that the exposed population on the whole increased in viability rather than the reverse. The effects on general viability are apparently due to hybrid vigour, due to the presence of freshly arisen mutations in heterozygous condition.

PARENTAL AGE EFFECTS ON MAN

Eeva Jalavisto
Institute of Physiology, Helsinki

The life expectancy of offspring in relation to parental age has received very little attention. This is easily understood because of the difficulties in the collection of material suitable for such a study. In official vital statistics the dates of birth of the parents are not recorded, and the only feasible method is to compile data from family records. Holmes and Wilson (1925) and Holmes (1928) have collected material from European royal lineage, but although it extends over about eight or nine centuries the data are nevertheless rather scanty. Holmes and Wilson showed that the life expectancy at 20 years is not dependent upon maternal age if families of the same size only are compared. However, on the whole the older brothers tend to live longer than their younger brothers. The same relationship was shown by Beeton and Pearson (1901). Ansell (1874), Yerushalmy (1938, 1939), Gardiner and Yerushalmy (1939), Burns (1942), Tabah and Sutter (1948) and Hoogendoorn (1953), amongst many others, clearly demonstrated that the age of the mother influences the rate of stillbirths and early postnatal mortality. With increasing age of the mother the death rate of children under one year of age increases steadily even in children of the same birth order (Yerushalmy, 1938, 1945), but the question of the postnatal mortality is controversial, the opposite relationship also being found (Heady *et al.*, 1955; Knox and Mackintosh, 1958). For references MacMahon and Gordon (1953) may be consulted.

Material and Methods

The material to be presented was collected from Swedish and Finnish published family records (Jalavisto, 1950, 1951).

It comprises 17,986 cases in which the years of birth and death of the children as well as those of their parents were known. The families were therefore completed when recorded. All cases of violent death were excluded. The material goes back to the 16th century, but most of it is from the 18th and the first half of the 19th century. Most cases come from

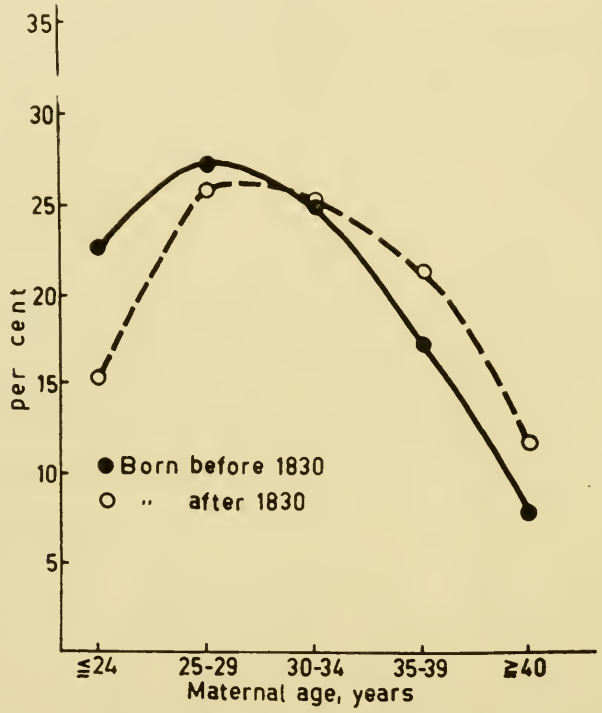


FIG. 1. Percentage of cases in various maternal age groups of children born before and after 1830, respectively.

Finnish middle-class and noble families, the rest from Swedish middle-class and noble families. The social level is thus rather high. The life expectancy is calculated as mean age at death minus the years lived.

The time of observation must be at least 100 years if correct values for the entire expectation of life are to be recorded. However, this necessarily implies inconsistency in the material, caused by changing environmental conditions during such a

long time period. In this study, therefore, no attention has been paid to observance of the 100-year span. The expectation of life was calculated for different maternal ages at the birth of the children, notwithstanding the excess of short-lived among those born in the latter half of the 19th century. It was assumed that this would give erroneous absolute values for the total expectation of life but that it would not affect the parental age effects. In order to determine whether

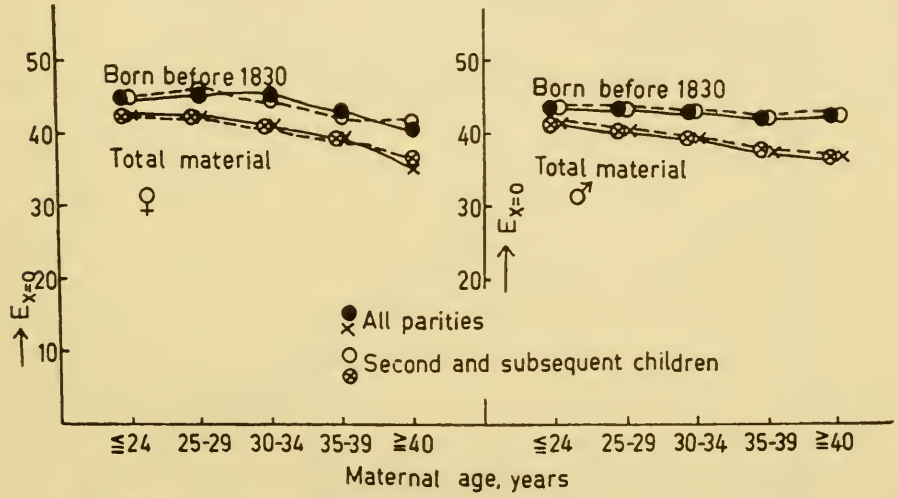


FIG. 2. Mean length of life ($E_{x=0}$) in various maternal age groups of boys and girls born before 1830 (12,786) and in the whole series (17,986).

this assumption was justified the relative number of the mothers in various maternal age groups, in those born before and after 1830, respectively, was calculated. The result is shown in Fig. 1. As may be seen, the distribution is not uniform: among those born after 1830 the number of young mothers is smaller than in those born before 1830. The deficit is evenly compensated for by the other maternal age groups. This means that there is a bias in the expectation of life in favour of the progeny of the youngest mothers. Fig. 2 records the expectation of life calculated for those born before 1830 and for the whole material. It seems evident that most

of the decrease in mean length of life is due to inconsistency in the distribution of young and old mothers. Whether other factors were operative, possibly in the reverse direction, during the earlier centuries is difficult to assess. It seems essential, therefore, to avoid calculation of the entire expectation of life and to search for some other method of study.

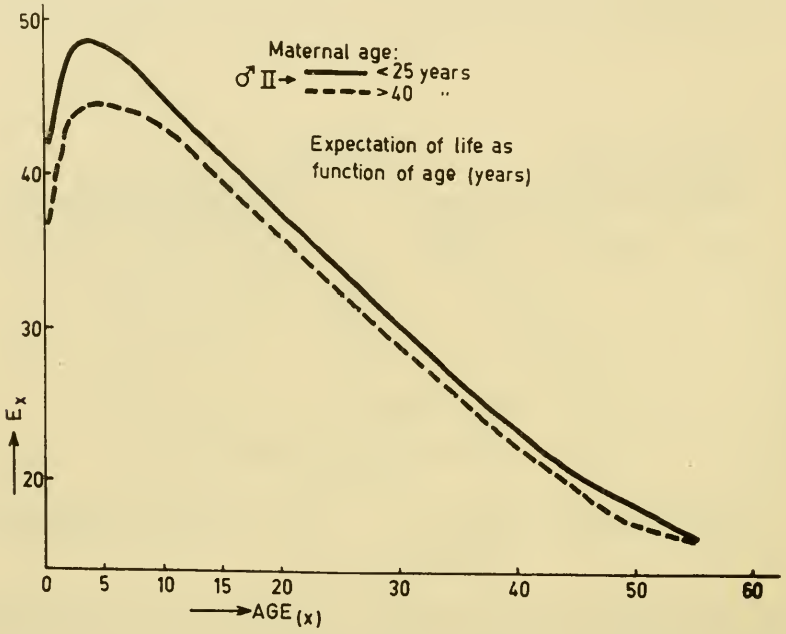


FIG. 3. Expectation of life (E_x) as function of age in the male progeny of young (<25 years) and old (>40) mothers; first-born excluded.

However in one respect the expectation of life calculated for each age and for different maternal age groups is instructive. Fig. 3 shows the expectation of life as a function of age for the progeny of young and old mothers (first-born excluded). It may be noted that from 6 years of age onwards the difference in expectation of life between the progeny of young and old mothers begins to diminish and between the ages of approximately 15 to 40 years the difference is constant. This can be interpreted as evidence that at least in the middle-aged the

maternal age does not affect the mortality. Therefore, it should be possible to use a group between the ages of 15 and 40 years as a basis of reference when the maternal age effects have to be elucidated. The frequency of births in different age groups cannot be determined directly because of the fictitious nature of the population to be studied. Since only cases of death are recorded, variations in death rate affect the age structure of such a population. Furthermore, since the material comprises data from individuals whose birth may be several centuries apart it would not be possible to use data given by vital statistics. The distribution of births varies in different historical periods and for Finland the births grouped according to the age of the mother are given only from 1871 onwards. The present author therefore thought that since the mortality in the age group 20–29 years is probably not affected by maternal age the percentage distribution of cases of this age would reflect the frequency of births in the different maternal age groups. If similar percentage distribution curves are constructed for ages at death below 6 years of age a possible parental age effect would manifest itself in an excess of cases in one of the maternal age groups, and this is what is actually seen. Fig. 4 gives the distribution of cases in various maternal age groups. As can be seen, the curves representing deaths during the first and the second years of life have a different course from all the other groups studied. The maternal age group of 25–29 years seems to be particularly favourable for the infants whereas the maternal ages over 35 years seem to have an excess mortality of infants less than 2 years of age. If the distribution of cases is studied by the χ^2 method it shows that the distribution of deaths of children under 2 years, from 2 to 19, and between 20 and 29 years, of these maternal age groups, differs from a random distribution quite significantly: $\chi^2 = 25{\cdot}7$ (degrees of freedom $= 6$) $P < 0{\cdot}001$. If, however, deaths at 2–4 years are examined it may be noted that the distribution of deaths in this age resembles more closely the distribution of deaths in the 20–29 year group than

that in the group under 2 years old. Furthermore, if a group is formed containing the cases of 2–19 years it differs from the 20–29 years of age group only slightly, the probability for random occurrence being $0{\cdot}05 > P > 0{\cdot}02$. Since the age group 20–29 is small, the age group 2–29 years may be used as the basis of reference.

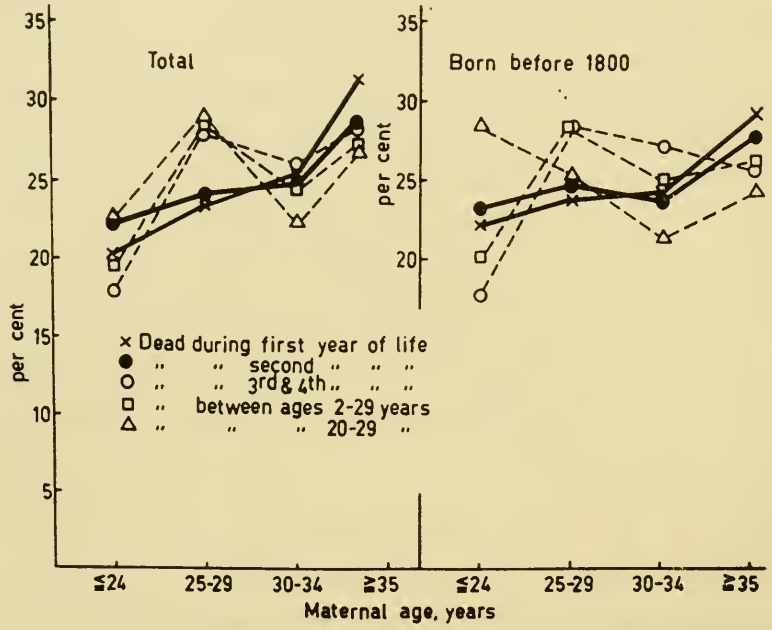


FIG. 4. Distribution in various maternal age groups of deaths of children under 30 years of age. Total series, 5,590 cases; 2,735 were born before 1800.

It may be asked whether the difference found is a real one, or could be due to differences in recording, i.e. due to the fact that in the latter part of the 19th century the number of recorded infant deaths is relatively greater than in earlier years. In order to exclude this fallacy, the same comparison has been made with cases born before the year 1800. The result is exactly the same except that the number of cases in the 20–29-year group is rather small and gives a somewhat abnormal distribution of deaths. The 2–29-year group is

therefore to be preferred as an indication for the distribution of births in this population. Since on an average only 29 years separate the deaths occurring during early infancy from this "standard distribution" it is not conceivable that differences in external conditions could affect the result. The conclusion would therefore seem to be that a maternal age of over 35 years increases the mortality of the progeny during the first two years of life. The optimum age with the least deaths is that of 25–29 years of age. Beyond early infancy, namely between the ages of 2 and 4 years, the effect of advanced maternal age is already quite small or non-existent, and it cannot be demonstrated in older groups, either because there is no influence or because of methodological difficulties arising out of incompatibility of life-expectancy data collected from an over-long (at least 100 years) time period.

No mention has so far been made of the possible rôle of paternal age effects. Since maternal and paternal ages tend to be correlated the question is rather intricate. If the material is divided into paternal age groups and a dependence of life expectancy or infant mortality on paternal age is recorded, this may simply reflect the effect of maternal age. If on the other hand no difference is noted, then the paternal effect possibly acts in the opposite sense to the maternal age, high paternal age being favourable for the progeny. Curiously enough, in the total material, in spite of the bias shown to arise from the different distribution of young and old mothers in the material collected before and after 1830, no paternal age effect upon the total expectation of life could be demonstrated. The most probable explanation would be that maternal and paternal ages may after all not be strictly correlated. The rather large mean difference found between the age of spouses (7–10 years) obviously allows fairly wide discordant variations in the material considered here. The same objections can, however, be made against calculation of the total expectation of life in the paternal age series as in the maternal series. Therefore the same procedure for elimination

of external bias arising from the 100-year time span necessary for studies of total life expectancy has also to be applied in the paternal age series.

The percentage distribution of deaths at various ages (0, 1, 2–4, 20–29 and 2–29 years) in different age groups of fathers is calculated. The paternal age groups are formed so that the limits are five years higher than in the maternal series, and the

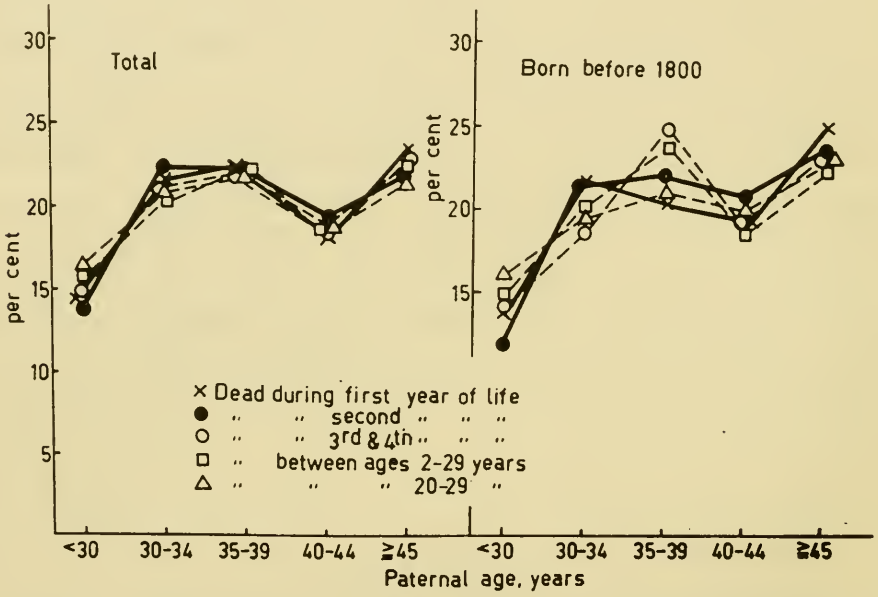


FIG. 5. Distribution in various paternal age groups of deaths of children under 30 years of age. Total series, 5,590 cases; 2,735 were born before 1800.

last group extends ten years beyond the highest maternal age group.

The result is seen in Fig. 5. It may be seen at a glance that differences in paternal age do not affect the distribution of cases at any age: there is hardly any excess of infant deaths with fathers of advanced ages. The difference between the maternal and paternal age distribution of infant deaths strengthens the impression that the maternal age effects are not artifacts, and that this method of study is practicable.

Discussion

One-third of the total material is made up of deaths under the age of 30 years (5,590 cases). These are, however, divided into several parental age groups and groups with different ages at death. The cases in a group are thereby reduced to quite a small number, always less than a thousand and sometimes as low as 200. A further reduction, e.g. resulting from grouping according to birth order, would not give relevant information because of the smallness of the material. Since parity and maternal age tend to correlate it is not possible to study the effects of birth order on infant mortality in this series. However, the main result of this investigation suggests that the maternal age effect is restricted to the first two years of life. It is therefore not necessary to use genealogical material for the elucidation of questions on the effects of parity, etc., since recent statistics are available and more appropriate for this purpose.

The difficulties when dealing with family histories are many, and lie mostly in their heterogeneity. The only uniform feature is the rather high social rank of the families. Family records of labourers' or peasants' families, for example, are rarely available. The advantage of the uniformity is, however, lost by the necessarily long time period, usually covering several centuries, needed to compile a population sample of a sufficient size. During such a long period of time famines, epidemics, general hygiene and the standard of living have changed and influenced mortality rates and causes of death.

The results concerning maternal age effects are rather controversial. Whereas there is agreement concerning perinatal mortality, which increases with age of the mother, infant mortality is found sometimes to increase and sometimes to decrease with maternal age. When family histories have been used for investigation of effects on longevity a slight deleterious effect of advanced maternal age has usually been found. Gibson and McKeown (1950) have pointed out that

favourable economic circumstances in the population studied tend to eliminate the maternal age effects, which may explain the discrepancy between earlier and more recent data. In spite of the high social level of the family histories on which this study is based they represent a population with a very high mortality. It is quite obvious that if a maternal age effect exists, it is never very pronounced. Therefore it is easily understood that low mortality in favourable conditions does not allow such small effects to manifest themselves. Consequently recent population statistics in western "Welfare States" can no longer be used for detection of maternal age effects. However, there still exist countries with sufficiently low standards of living for such studies. It would be interesting to compare records from these countries with data from countries with a high standard of living.

Summary

Parental age effects were studied in material comprising 17,986 cases collected from Scandinavian noble and middle-class family histories. It was concluded that total expectation of life is not suited for elucidation of such effects, because of the necessarily extended period of observation with resulting inconsistency of the data. Since, however, such calculation made it probable that advanced maternal age had no effect on deaths after the age of 15 years, the group of dead between the ages of 20 and 29 could be used as indicative of the frequency of births in different parental ages. When the distribution of dead during the first and second years was compared to that in the 20–29 year group, a slight excess of infant deaths during the first and second years of life was noted in the highest maternal age group ($\geqslant$ 35 years). In the maternal age group 25–29 years the relative number of infant deaths was remarkably low, this maternal age being the most favourable for the survival of the offspring. A similar comparison in the paternal series did not show any significant paternal age effect on the survival of the progeny.

REFERENCES

ANSELL, S. (1874). Quoted by MacMahon and Gordon (1953).
BEETON, M., and PEARSON, K. (1901). *Biometrika*, **1**, 50.
BURNS, C. M. (1942). Quoted by MacMahon and Gordon (1953).
GARDINER, E. M., and YERUSHALMY, J. (1939). *Amer. J. Hyg.*, **30**, 11.
GIBSON, J. R., and MCKEOWN, T. (1950). *Brit. J. soc. Med.*, **4**, 221.
HEADY, J. A., DALY, C., and MORRIS, J. N. (1955). *Lancet*, **1**, 395.
HEADY, J. A., STEVENS, C. F., DALY, C., and MORRIS, J. N. (1955). *Lancet*, **1**, 499.
HOLMES, S. J. (1928). *Univ. Calif. Publ. Zool.*, **31**, 359.
HOLMES, S. J., and WILSON, I. (1925). *J. Hered.*, **16**, 47.
HOOGENDOORN, D. (1953). *Ned. T. Geneesk.*, **97**, 2130.
JALAVISTO, E. (1950). *Rev. méd. Liège*, **5**, 719.
JALAVISTO, E. (1951). *Ann. Med. intern. Fenn.*, **40**, 263.
KNOX, G., and MACKINTOSH, J. (1958). *Brit. J. prev. soc. Med.*, **12**, 131.
MACMAHON, B., and GORDON, J. E. (1953). *Amer. J. med. Sci.*, **226**, 326.
TABAH, L., and SUTTER, J. (1948). *Population* (*Paris*), **3**, 63.
YERUSHALMY, J. (1938). *Amer. J. Hyg.*, **28**, 244.
YERUSHALMY, J. (1939). *Hum. Biol.*, **11**, 342.
YERUSHALMY, J. (1945). *Hum. Biol.*, **17**, 65.

DISCUSSION

Sacher: Aren't many of the early deaths at present due to congenital defects and could that be strongly related to parity ?

Jalavisto: In young mothers the mortality rate increases according to their parity, but in older mothers that does not matter so much.

Sacher: So you do not think that parity is a major factor ?

Jalavisto: It might be.

Rockstein: There are two distinct ways in which parental age may affect the offspring. There are the direct effects upon the foetus, which might possibly be environmental, and there are those upon the overall longevity of the successful offspring, which might be hereditary. In the housefly, for example, the effect of the advanced age of the parent upon the effective potential of the total population is deleterious, primarily through fewer eggs, of lesser viability, being produced by older parents. On the other hand, where we do have surviving offspring, the longevity of the male housefly is extended considerably (by about 20 per cent). We may likewise have two distinct effects in human populations: where an offspring of an older parent survives, i.e. where an old mother successfully produces young, the young will be longer-lived. The mother in this way may be selecting (or producing a selective effect upon the

population) to the extent that she is herself a long-lived individual. That is, she may be still fertile at the age of 40 or 45 and producing a large family. These offspring will then be long-lived by virtue of this and the net effect will be not to have an adverse effect upon the successful offspring. In other cases, offspring from older parents will be stillborn or malformed at birth. However, Sonneborn has analysed the statistics for a large population of offspring from the New York City vital statistics records. He found that there was a stronger correlation, in a positive sense, between *paternal age* and the number of stillbirths, than with maternal age. This is usually ignored in the statistics, because normally the age of the mother is known rather than the age of the father.

Berg: Was the normal lifespan about 45 years in 1800 ?

Jalavisto: Yes.

Berg: That would be before the onset of diseases of senescence. Causes of death were chiefly physical or infectious in nature.

Danielli: There are three distinct factors which might affect the mortality of the children. First, there may be changes in the Mendelian characteristics transmitted through the chromosome material. If it were true that there were no parental effects, one would think that no type of deterioration of the chromosome genes was contributing to your results, Prof. Jalavisto. Second, there is the possibility that you may get cytoplasmic inheritance effects coming in. Then, of course, the actual environment to which the embryo is exposed is also changing as the age of the mother changes, but not as the age of the father changes. So the mother has two chances (or three, if cytoplasmic inheritance effects are included) of altering the expectation of life of the child, whereas the father has only one chance.

Maynard Smith: Even in organisms without placentae, e.g. *Drosophila*, there is plenty of evidence that the age of the female laying an egg will influence the probability that this egg will hatch. In human data one might suppose that the age of the mother, through the cytoplasm of the egg she produces, influences the rate of stillbirths. There is no difficulty in supposing that either egg cytoplasm or uterine environment might influence the survival during the first two years of life, but they are less likely to influence long-term survival.

Danielli: To what extent are more children surviving in recent years from older mothers than was the case 100 years ago ? If more are indeed surviving, the shift to the right of the final curve in Dr. Benjamin's death curves might be due to such an effect.

Comfort: There are several social factors which affect the parental

age at first birth, and there must be considerable differences in its distribution now, compared with populations where parenthood was not so optional. Children born to very young mothers now are often also socially underprivileged or illegitimate. But in spite of this, they have a statistically better performance than first children born to predominantly prosperous mothers between 35 and 40 (Baird, D., Hytten, F. E., and Thomson, A. M. (1958). *J. Obstet. Gynaec. Brit. Emp.*, **65**, 865). There is also the point in regard to parental age effects that when there are very large disparities in age between husband and wife, the proportion of cases where the husband is not the father increases very considerably.

Maynard Smith: There is another point on this genetic question of whether, if more old mothers are having children which survive, this could have a genetic consequence on the expected longevity of a population. It would be very dangerous to assume without evidence that there will be a positive correlation between the longevity of parents and offspring. Beeton and Pearson (1901) found a correlation, but it was very small compared with, for example, the correlations for stature or for other metrical characters. There are genetic reasons why one might expect, for a character closely associated with fitness, to get small parent-offspring correlations. Certainly Dr. Comfort and I in independent work have found low parent-offspring correlations for longevity in *Drosophila*. Yet Prof. Rockstein has implied that he gets quite a considerable correlation in the housefly, for the male offspring only. We require better evidence in the human population as to whether there is or is not a high correlation between the longevity of parents and their children.

Danielli: We do not really know whether there are significantly more children of older parents surviving, because once there is a probability through advancement in social techniques that a woman of potentially childbearing capacity will survive longer, then her opportunities for not having children, so to speak, also increase and this effect may be working in the opposite direction. So unless we have actual evidence on this point, we have not even got the raw material to find out whether there is any genetic effect at all.

Mühlbock: In our inbred mice some of these factors are not apparent. We can control the genetic constitution equally well in all the animals. We observed first that there are more deaths *in utero* with a higher age and that the litter size is also much smaller. This is not just the effect of the number of eggs, but it is also a uterus effect. Maybe the hormonal stimulation in the endometrium of the uterus is not good enough in old age. Then we tried to find out whether the lifespan of these inbred mice is influenced by the age of

the mother. We did that with the C57 black strain. We considered the lifespan only of female animals living longer than one year, i.e. half the usual lifetime of a mouse. The fertility age of this strain is up to twelve months. We divided the offspring according to the age of the mother, first three months, then four to six months, and then six to twelve months. There was no difference in the lifespan of these offspring. The environmental factors were the same and there is no difference in genetic make-up.

Berg: We have been able to extend the age of fertility considerably in the rat, by regulating the food intake. For example, 700-day-old female rats fed *ad libitum* have a fertility rate of 12 per cent. On a controlled food intake fertility is increased to 67 per cent.

Jalavisto: One feature of these family records is that the families are very big. There are great age differences between the members of one family, although the environment is fairly consistent.

Hinton: Your main maternal effect may be restricted to the first two years of the life of the offspring partly because the older mothers have more experience. For example, we have children 17 years apart, and we took care of our later children much better than we did of the first ones.

Comfort: Even so I think there is a higher early death rate among first babies born to prosperous mothers over 40 than among those of underprivileged mothers of 18. I doubt if this is entirely a matter of maternal experience.

Jalavisto: I have divided the material into first and second children and there is no difference. The second and subsequent children show the same effect as the first children.

Danielli: It may just be that the mothers do not bother so much with the later children.

Benjamin: The present discussion does seem to tie in with what Dr. Berg said earlier about deaths of children being due to acute infections or other endogenous diseases. This factor of the experience of the mother helping her to deal with infections would seem to be important. You would find great difficulty in making such researches in this country now, because there seems to be a strong tendency for women to have their children very young and very early in married life.

Jalavisto: In Finland we have on record what is probably the highest maternal age—a woman nearly 60 years old!

STUDIES ON THE LONGEVITY AND MORTALITY OF ENGLISH THOROUGHBRED HORSES*

A. Comfort

Department of Zoology, University College, London

The General Stud Book records the year of foaling, and in many cases the year of death or disposal, of the thoroughbred racehorses foaled in Britain since the end of the 18th century. This record has been compiled with careful attention to identity, and is greatly superior in quality and quantity to the other non-human mammalian vital statistics so far examined. The possibility of using it as a source of biological data has been recognized before (e.g. Vitt, 1949) but never fully exploited, chiefly, no doubt, because for most purposes each life history must be individually extracted, and statistical treatment of a large sample is therefore very slow work.

Since actuarial figures for large mammals are scarce and theoretically important, the Stud Book has been examined to see how far it could be expected to yield useful material for comparative age studies, especially in relation to parental age effects and the inheritance of longevity. Study of parental age effects on lifespan in man is complicated by the high correlation between ages of spouses (Sonneborn, 1957); there is no such correlation between ages of sire and dam in horse-breeding, and both mares and stallions commonly remain at stud to advanced ages. One special object of the study was to examine Vitt's (1949) claim that the Stud Book records indicate a large parental age effect on the vigour and longevity

* The work described in this paper was carried out during the tenure of a Nuffield Research Fellowship in Gerontology. Part of it received a Ciba Foundation Ageing Award in 1958.

of thoroughbreds. Another was to see whether the records could be used to determine the extent of the parent-offspring and sib-sib correlations for lifespans.

The following account combines and summarizes the results already described elsewhere (Comfort, 1958*a*, *b*, 1959*a*).

Materials and Method

The Stud Book consists to date of 34 volumes, published at four-yearly intervals since 1808. It is essentially a nominal list of brood mares, giving details of the serving, foaling and ownership of each since the last entry. Arabian mares are listed separately.

From this record can be obtained (1) the year of birth of every thoroughbred foal under the name of its dam, (2) the life history of every filly which returns to stud as a brood mare, from her first covering by a thoroughbred stallion until death or disposal from the stud.

The life histories were extracted by following each individual animal by name from its first appearance as a brood mare until its last; in all, including those required to establish parental longevity, and additional lives scored in the course of coat-colour studies, about 10,000 histories were extracted in this way. Initial samples taken were (1) all the thoroughbred fillies foaled in Britain, excluding Ireland, in the years 1875–80 (Sample A) and 1860–64 (Sample B) which subsequently re-enter the record as brood mares, (2) all the Arabian mares foaled in 1880 and the 35 subsequent years—a compact group of manageable size, where over half the fillies returned to stud. The original six annual cohorts of thoroughbreds (Sample A) were chosen so that their survival period avoided the World Wars. After this sample had been analysed, Sample B was taken to obtain more data upon the relationship of longevity to parental age. The thoroughbred cohorts of 1900 and 1901 were scored later, to see whether secular changes had occurred in the course of the record.

Each life history normally ends in an entry that the animal was shot, died, was exported, or was disposed of (put out of stud, sold, given away as barren). Some end in unexplained disappearance from the record or in "no further return". Each unaccounted absentee was sought by name in each volume to the end of a 32-year period from its year of foaling, and for two volumes thereafter to allow for corrections.

The forms used in the terminal entries are "died", "shot", "sold", "sent abroad", and qualifications of these, e.g. "broke leg and shot", "died after foaling" (the last of these implies only that the mare had foaled, not that foaling was the cause of death). The entries therefore discriminate between losses to the record, deaths due to accident, animals destroyed, and deaths presumed to be due to natural causes; but of animals entered as "died" only those dying at or after foaling, and of animals shot only those which met with an accident, are usually distinguished. Deaths not attributed to accident or shooting account for 1,009 out of the total 2,742 lives in the cohort samples. Only these, which include deaths at or after foaling, were scored as "natural" (d_x) in computing the age-dependent mortality, all other losses, and all animals dying at imprecise ages, being scored as lost to the record (a_x). Where the last surviving individual is lost to the record, it is assumed to have died in that year.

Life-tables from 4 years of age were then prepared by calculating the yearly mortality under this convention, with the usual correction for losses. Details of the calculation have been given elsewhere (Comfort, 1958*a*). Standard errors of the expectation of life were obtained by Irwin's (1949) approximation.

Results and Discussion

General form of the survival curve

Survival curves drawn for the 2,742 thoroughbred mares in samples A and B, and the tabulated figures from which they

are derived, are given in Fig. 1 and Table Ia and b. The curves for the samples coincide closely; they are of typical Gompertzian form, with a high early survival and a steadily increasing force of mortality. The modal age of adult death

Table Ia

LIFE-TABLE FOR 1,492 THOROUGHBRED MARES, FOALED 1875–80

Year interval	d_x	a_x	q_x	L_x	*Corrected deaths* (10,000)	e_x
4–	4	11	0·0027	1·0000	27	17·043
5–	7	49	0048	9973	48	16·04
6–	11	48	0079	9925	78	15·05
7–	16	56	0120	9847	118	14·06
8–	20	69	0159	9729	155	13·08
9–	15	48	0127	9574	122	12·12
10–	18	50	0162	9452	153	11·17
11–	17	45	0162	9299	151	10·23
12–	19	42	0194	9148	178	9·31
13–	22	35	0237	8970	213	8·40
14–	23	43	0265	8757	233	7·51
15–	36	40	0448	8524	382	6·65
16–	33	37	0452	8142	369	5·82
17–	37	34	0560	7773	436	5·02
18–	41	41	0699	7337	513	4·26
19–	32	49	0639	6824	436	3·56
20–	31	52	0742	6388	474	2·90
21–	40	40	1173	5914	694	2·28
22–	61	38	2328	5220	1216	1·72
23–	34	33	2054	4004	822	1·26
24–	24	25	2342	3182	744	0·90
25–	12	24	2222	2438	542	0·62
26–	10	11	4082	1896	774	—
27–	2	2	2500	1122	280	—
28–	—	1	0·0	0842	0	—
29–	1	1	2857	0824	241	—
30–	—	2	(1·0)	0601	601	—
31–	—	—	—	0·0	—	—
n=	566	926			10,000	

$V_e = 0·046$
$\sigma_e = 0·214$
Standard deviation = 5·5 yrs.

is 22 years. The proportions are very like those of prosperous human survival curves; the time equivalence, obtained by fitting the median and second quartile to the U.S. Census curve for white males, 1941, beginning at the age of 10, is

Table Ib

LIFE-TABLE FOR 1,250 THOROUGHBRED MARES, FOALED 1860–64

Year interval	d_x	a_x	q_x	L_x	*Corrected deaths* (10,000)	e_x
4–	—	1	0·0	1·0000	—	17·314
5–	3	15	0024	1·0000	24	16·31
6–	4	30	0033	9976	33	15·32
7–	11	55	0094	9943	93	14·23
8–	16	48	0145	9850	143	13·33
9–	14	80	0136	9707	122	12·35
10–	16	59	0170	9585	163	11·41
11–	18	45	0206	9422	194	10·44
12–	8	50	0099	9228	91	9·50
13–	23	37	0303	9137	277	8·57
14–	25	41	0359	8860	318	7·69
15–	23	25	0360	8542	308	6·82
16–	29	30	0493	8234	406	5·98
17–	25	31	0473	7828	370	5·17
18–	33	41	0706	7458	527	4·41
19–	32	36	0808	6931	560	3·69
20–	30	33	0910	6271	580	3·03
21–	33	38	1250	5791	724	2·42
22–	35	31	1718	5067	902	1·87
23–	19	22	1407	4165	586	1·41
24–	22	24	2366	3579	847	1·03
25–	15	18	3000	2732	820	0·71
26–	6	9	2791	1912	534	—
27–	1	5	1176	1378	162	—
28–	1	1	2222	1216	270	—
29–	1	1	4000	0946	378	—
30–	—	1	1·0	—	568	—
$n=$	443	807			10,000	

$V_e = 0·044$
$\sigma_e = 0·214$
Median = 22·07 yrs.

roughly $\times$ 3·2. The last part of the curve calculated from q_x values at ages of 25 and over is, of course, largely arbitrary, and in the late intervals losses, many of them from age-dependent causes, equal or exceed deaths.

The survival curves and expectations of the separate cohorts are roughly similar, but there is substantial scatter (Table II),

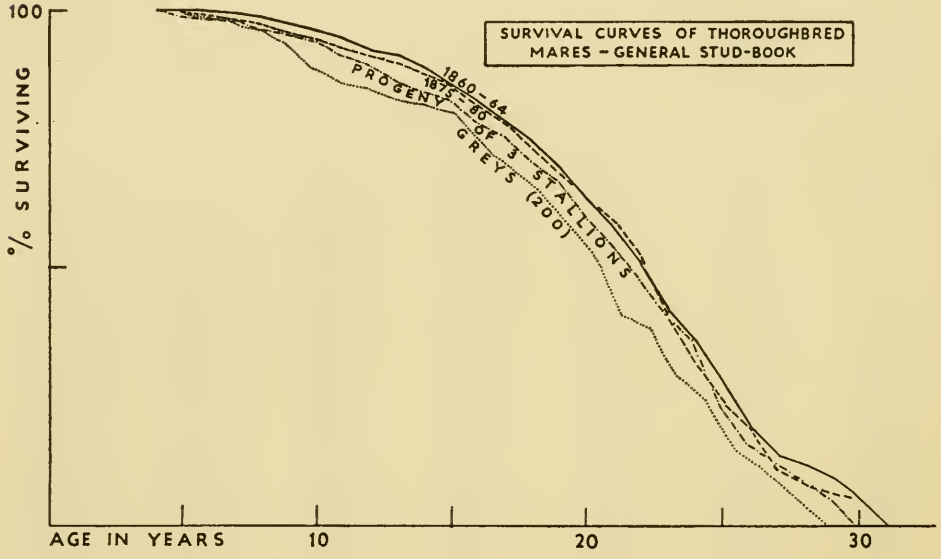


FIG. 1. Survival curves of mares foaled in 1860–64 (———), in 1875–80 (– – – –), of brood mares by three selected long-lived stallions (Hampton, Galopin and Hermit) (— · — · —), and of grey mares (.....).

the last three years of the 1875–80 sample having a shorter expectation of life than any of the others ($0{\cdot}05 < P < 0{\cdot}02$ for the largest difference). The proportion of scoreable lives to total fillies foaled is rather higher in sample B (33·0 against 26·8 per cent) but there is no immediately obvious reason for the differences in cohort performance. There may be bias in sampling, since the two lowest-scoring cohorts of sample A contain an unusually low proportion of late entrants to the record. Mares are normally entered when first covered, but animals among the unaccounted majority which have not

Table II

LONGEVITY OF THOROUGHBRED MARES BY YEARS OF BIRTH

	Number scored	*Total year's fillies*	%	*(Years)* $e_{x=4}$	V_e	*Median*
1860	242	726	33·33	17·44	0·21	22·70
1861	255	763	33·42	17·28	0·18	21·86
1862	244	757	32·23	17·33	0·35	21·82
1863	241	783	30·78	16·58	0·21	21·62
1864	268	756	35·45	17·39	0·17	22·03
1860–64	1250	3785	33·03	17·31	0·044	22·07
1875	285	910	31·32	17·26	0·34	22·43
1876	245	863	28·39	17·64	0·21	22·43
1877	233	915	25·46	17·44	0·21	22·49
1878	248	969	25·59	17·49	0·30	22·15
1879	261	952	27·42	16·13	0·16	20·81
1880	221	954	23·17	16·01	0·18	21·81
1875–80	1492	5565	26·82	17·04	0·046	22·18
1900	501	1674	33·41	15·20	<0·1	19·55
1910	650	1566	41·50	15·11	<0·1	20·65
Arabians 1880–1915	183	314	58·26	18·81	0·43	23·66

THOROUGHBRED MARES—LONGEVITY AND SURVIVAL BY COAT COLOUR

Group	*n*	$e_{x=4}$	V_e	*Median*
Bays (1875–79)	568	16·68	0·08	22·03
Blacks (1854–1900)	358	16·53	0·15	21·95
Chestnuts (1875–79)	262	17·23	0·20	22·50
Greys (1845–1920)	200	15·57	0·28	20·43

been regularly at stud may enter the record at any age if they produce a thoroughbred foal; some of these have probably been missed. But on the basis of mortality rates calculated for all the cohorts at 4 years of age, omitting subsequent entrants, it appears that this bias is only enough to account for a small part of the difference observed. The 1900 and 1910 cohorts gave much lower figures for mean and median expectation of life than either of the earlier samples. This apparent fall in performance might be influenced (1) by the 1914–18 war: the increased losses are concentrated early in the 1910 table and about 10 years later in the 1900 table, (2) by a change in breeding policy—mares over 23 are rare in recent volumes, being now apparently put out of stud at earlier ages. A secular trend in lifespan cannot be assumed without scoring further cohorts, but there is some *prima facie* evidence of it here.

The mean expectation of life of Arabians was significantly higher than that for any cohort of thoroughbreds ($e_{x=4} = 18{\cdot}81 \pm 0{\cdot}66$ years) and the rate of decline slower. These lives are spread too thinly over too long a period for any secular trend to be made out.

Maximum age records

The highest ages in the series were reached by Arabians, three mares reaching 31 years, and one dying in its 33rd year (born 1911, died 1943; last covered, but barren, 1942); these ages may only indicate more conscientious returns for Arabians past breeding age, compared with thoroughbreds. The two oldest thoroughbred mares in the sample were alive at 30 years. The Stud Book has not been searched in detail for higher records—the oldest mare so far encountered (Blue Bell, by Heron out of Jessie) was foaled in 1851 and died in 1885 at the age of 34. Pocahontas (Stockwell's, Rataplan's and King Tom's dam) was foaled in 1837, died in 1870, and bore her last foal in 1862. The frequency with which such ages are

actually reached by thoroughbred mares is largely determined by human intervention, since many which disappeared from the record at ages of 25 or over were probably capable of living longer—some no doubt did so, dying unrecorded. The stallion Matchem (1749–1781) reached a reputed age of 33; in the obituary lists of the Stud Book one other stallion reached 32, and four reached 31.

These ages agree with maximum authenticated records in other breeds (Hokkaido ponies 32+, Matsumoto, 1935; Hafling mares, over 32, Schotterer, 1939; Lipitsa horses ♂31, ♀33, Kadić, 1949). Claims of higher ages have been reviewed elsewhere (Comfort, 1956). Many of these refer to ponies, and none is supported by Stud Book records. Thirty-eight years is recorded in a captive zebra (Weber, 1942).

Effects of parental age on the longevity of progeny

Vitt (1949) has claimed that the longevity and racing performance of thoroughbred horses are substantially influenced by the age of both dam and sire, and that impairment of vigour by the use of old breeding stock is cumulative. He found that in a sample of 100 mares from the early years of the General Stud Book, the progeny of dams twelve years old or less developed more slowly, judged by the age at first foaling, and lived longer ($e_{x=4} = 19 \cdot 5$ years) than the progeny of dams aged 13 or more ($e_{x=4} = 16 \cdot 4$ years). Absolute figures and standard errors are not given, and it is not clear whether the estimates are corrected for losses or based on the distribution of recorded deaths alone. Vitt also compared the fertility and racing form of foals by old and young stallions, and concluded that there was an equally marked paternal age effect, the optimal performance being reached by the foals of stallions 8–16 years old out of mares 6–13 years old.

To test this the lives in sample A were distributed (a) by age of dam at foaling, (b) by age of sire at covering, one year earlier, (c) by age of dam at foaling and sire at covering, where

these fell in the same grouping interval. Of 1,492 lives, 1,342 were scored and grouped by age of dam, 1,355 by age of sire, and 719 by both, the missing lives among these being scored for one parent only—chiefly the progeny of imported horses, of stallions whose dates of birth were not easily ascertainable from the record, or of mares covered by more than one stallion in the season. The distribution of parental ages is shown in Fig. 2, and the results of the calculation in Table III.

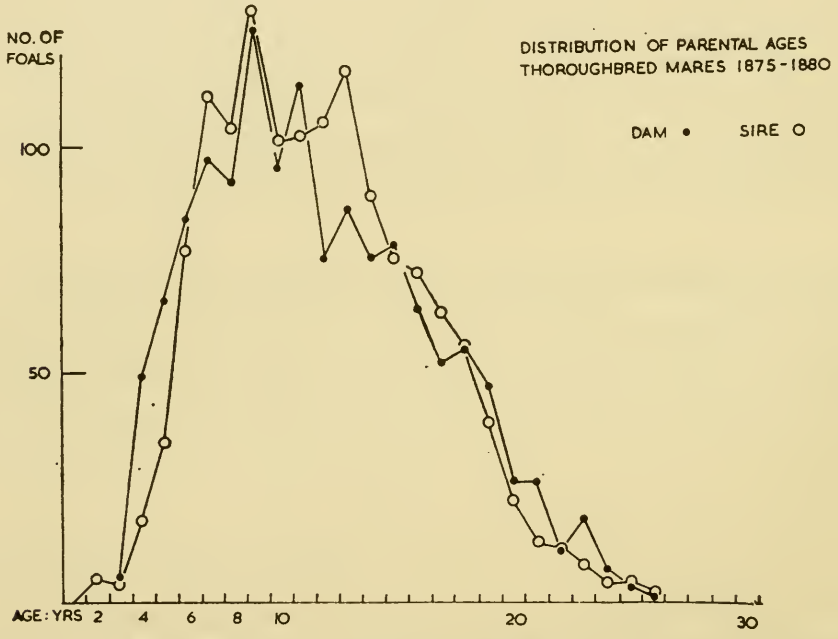


FIG. 2. Mares foaled in 1875–80: distribution of ages of sires at covering (○) and dams at foaling (●) (Comfort, 1958*a*).

Reproduced by courtesy of the Editor, *Journal of Gerontology*.

There was no significant difference in expectation of life between foals of mares under and over 13 years of age ($\leqslant$ 12, $e_{x=4} = 16{\cdot}89$; $\geqslant$ 13, $e_{x=4} = 16{\cdot}86$ years). With further subdivision the progeny of the oldest mares had the shortest lifespans, but the largest difference was less than twice its standard error. Still smaller differences were obtained for the same lives grouped by paternal age alone. Of the 719 lives grouped by age of both parents, those whose dam and sire

Table III

LONGEVITY OF THOROUGHBRED MARES BY PARENTAL AGES
(SIRE AT COVERING, DAM AT FOALING)

	n	$e_{x=4}$	V_e	(*Years*) *Median*
Whole sample				
Foaled 1875–80 (A)	1492	17·04	0·046	22·18
,, 1860–64 (B)	1250	17·31	0·044	22·07
Mares foaled 1875–80 (*Sample A*) *and* 1860–64 (*Sample B*) *Dam* (Sample A):				
under 8 yrs.	297	16·90	0·12	21·07
8–12	537	16·66	0·09	21·06
13–16	303	17·29	0·17	22·21
⩾ 17	248	16·15	0·23	22·83
Sire (Sample A):				
under 8 yrs.	250	16·73	0·16	22·10
8–12	537	17·11	0·10	22·35
13–16	352	17·26	0·20	21·83
17–19	151	16·87	0·28	22·08
⩾ 20	65	16·87	0·73	21·03
Dam and sire:				
⩽ 12* Sample: A	449	17·39	0·22	22·28
B	531	17·07	0·11	21·90
A + B	980	17·33	0·07	22·10
⩾ 13* A	270	16·45	0·23	21·61
B	150	17·24	0·28	22·64
A + B	420	17·03	0·16	22·05
⩽ 9 A	128	17·91	0·22	22·28
B	220	16·51	0·27	21·50
⩾ 16 A	70	15·71	0·69	20·41
B	44	17·26	1·10	23·17
Progeny of Hermit, Galopin and Hampton				
All mares:	412	16·60	0·15	21·73
Got in or after sire's 20th year:	124	16·65	0·33	21·83
Got in or after sire's 16th year, dam ⩾16 at foaling:	41	16·29	0·89	21·19
All mares (*A, B and selected sires*) by parents ⩾16 yrs	154	16·45	0·38	21·12

* Include extreme groups (⩽9, ⩾16).

were under 13 years old lived slightly longer ($17 \cdot 39 \pm 0 \cdot 36$) than those whose parents were over 13 ($16 \cdot 45 \pm 0 \cdot 48$; $t \simeq 1 \cdot 4$, $0 \cdot 2 > P > 0 \cdot 1$), and the difference was greater in the extreme segments of these groups (dam and sire $\leqslant 9$, $17 \cdot 91 \pm 0 \cdot 47$; $\geqslant 16$, $15 \cdot 71 \pm 0 \cdot 83$; $t \simeq 2 \cdot 3$, $0 \cdot 02 > P > 0 \cdot 01$). This difference is much smaller than that described by Vitt from maternal age alone, and is of the order of the difference between cohorts.

In view of this result, the five additional cohorts (sample B) were extracted and scored for parental age, with the results shown in Table III. The differences found in the 1875–80 sample were not repeated here. The longest-lived group were the progeny of parents of 16 years and over, but the standard error was very large ($17 \cdot 26 \pm 1 \cdot 90$); the 220 animals which were the progeny of two young parents had numerically the shortest lifespans ($16 \cdot 51 \pm 0 \cdot 52$); none of the differences was significant, and all were in the reverse direction to those in the 1875–80 sample.

The mean expectations of life were also calculated for the foals sired early and late in life by three selected stallions: Hermit, by Newminster (1864–1890); Galopin, by Vedette (1872–1899); and Hampton, by Lord Clifden (1872–1897), for comparison with Vitt's analysis of the progeny of Swynford. These three stallions produced in their lifetime 141, 119 and 159 fillies which returned to stud. Forty-six, 13 and six of these came from the cohorts already scored, the remaining 347 being new lives. The combined curve of survival for all Hermit, Galopin and Hampton mares coincided closely with that for the original six cohorts; their mean expectation of life at 4 years was $16 \cdot 50 \pm 0 \cdot 39$ years. The 121 mares got during or after their sire's 20th year had a slightly, but not a significantly, higher expectation than the global mean ($16 \cdot 65 \pm 0 \cdot 57$) (Table III; Fig. 3). Only 41 mares were got by the three selected stallions in or after their 16th year upon dams 16 years old or more; these had a mean expectation of life of $16 \cdot 29 \pm 0 \cdot 94$ years. By combining these mares with the

progeny in samples A and B of parents 16 years old or over, 154 lives were obtained, with $e_{x=4} = 16{\cdot}45 \pm 0{\cdot}62$ years, which is less than any of the three global means, but not significantly so. These results, taken as a whole, seem to afford no good evidence of any consistent effect of parental age on the longevity of mares.

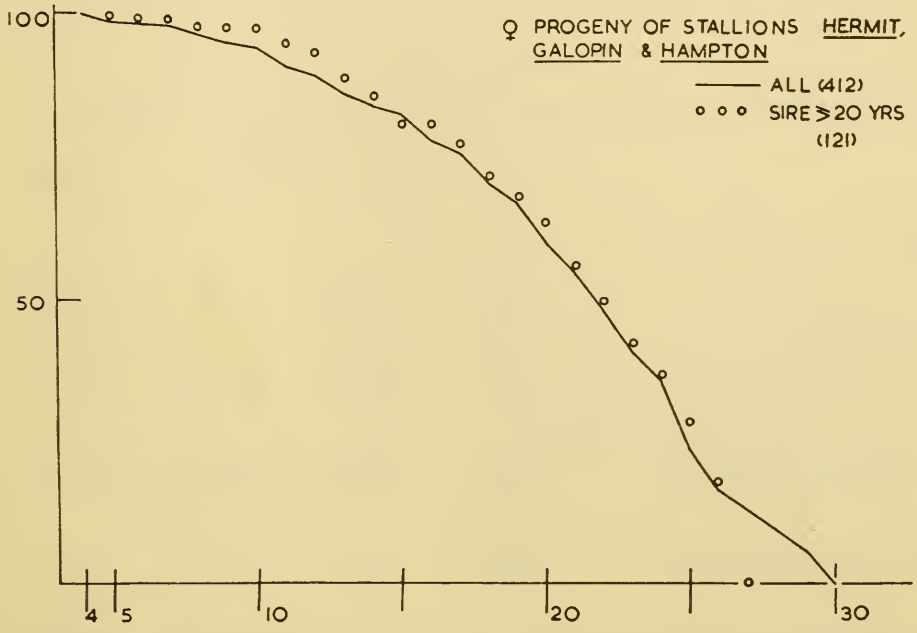


FIG. 3. Survival curves of lifetime brood mare progeny of Hampton, Galopin and Hermit (○———○) and of mares got in or after their sire's 20th year (Comfort, 1958*a*).

Reproduced by courtesy of the Editor, *Journal of Gerontology*.

Correlation between lifespans of parents and offspring

Since age of death depends in part upon heritable factors there should be a measurable difference in longevity between the foals of long-lived and short-lived parents, though Beeton and Pearson's (1901) results in man suggest that it would not be large. All the mares in sample A were scored for the longevity of their dam, and as many as possible for the longevity of their sire; the date of death could be ascertained only for stallions appearing in the obituary lists, or rather less than half

the sires contributing to the sample. Life-tables were made (a) for all the mares in sample A whose dams were known to have reached the age of 25, or died before the age of 14, (b) for mares in sample A whose sires reached 25 or died before 15, (c) for the female progeny of those mares in sample A which reached 25 or died before 14, (d) for 113 mares in the sample whose dam and sire both reached 23 years. The grouping limits in all

Table IV

LONGEVITY OF THOROUGHBRED MARES BY LONGEVITY OF PARENTS

	n	$e_{x=4}$ (*Years*)	V_e	*Median*
Mares foaled in 1875–80				
Sire reached 25 yrs.*	132	17·54	0·50	22·63
Sire died ⩽ 14	113	16·27	0·60	22·53
Dam reached 25 yrs.	238	16·96	0·16	22·25
Dam died ⩽ 13	53	16·35	0·59	21·18
Dam and sire reached 23 yrs.	113	18·07	0·34	23·74
Progeny of mares foaled in 1875–80				
Dam reached 25 yrs.	168	16·33	0·31	22·54
Dam died ⩽ 13	58	16·67	1·25	20·02
Progeny of Hermit, Galopin and Hampton				
Dam reached 24 yrs.	100	17·11	0·82	21·52
Dam died ⩽ 18 yrs.	58	15·39	0·83	21·51

* Stallions whose date of death appears in the obituary lists; mares by Hermit, Galopin and Hampton are excluded from this figure, but included in the figure for dam and sire ⩾ 23 years.

these cases were fixed to secure enough lives for the calculation; the relative contribution of short-lived mares to the sample was so small that it was not possible to prepare a table for the survival of their fillies by short-lived stallions. The mares by the three long-lived stallions, Hermit, Galopin and Hampton were also grouped by longevity of dam.

The calculated means (Table IV) show differences of less than twice the standard error in favour of all the groups with one long-lived parent, except the progeny of long-lived mares in the 1875–80 sample; the 113 mares with two long-lived parents had a mean expectation of life at 4 years of 18·07 ±

0·58 years, which is significantly more than the global mean, or the mean for any other group. The true difference is moreover likely to be minimized, since nearly half the dams and more than half the sires contributing to the global total died at unknown ages or from accidental causes, and these losses must include some potentially or actually long-lived pairs. The difference in lifespan of fillies by the three selected stallions out of long- and short-lived dams was about 1·3 times its standard error, but the short-lived mothers contributed only 53 lives, even when the grouping limit was raised to 18 years, and the comparison means little.

In view of Vitt's opinions, a table of the early progeny of long-lived parents was also made, taking all the available mares from all the scored samples whose dam and sire were aged 15 or less at the time of foaling or conception, but lived eventually to an age of 23 or more, thus avoiding competition between any age effect and inheritance of longevity. The performance of these mares was in fact numerically but not significantly poorer than that of the groups scored without regard to parental age ($e_{x=4} = 17 \cdot 09 \pm 0 \cdot 89$ years).

Coat colour

Five cohorts (1875—79) were scored for coat colour—of 1,271 mares composing them, 588 were bays, 181 browns, 262 chestnuts, 27 blacks, 5 greys, 3 roans and 2 grey-roans, the balance being of doubtful or unstated colour. In order to compare the less common coat colours, further records of greys and blacks were collected from other volumes of the Stud Book. Brown mares were excluded because of the heterogeneity of coat colours included under this description; so were all individuals of doubtful colour, e.g. "black or grey", at first registration.

Of the colours examined (Table II), only greys appear to diverge significantly from the means calculated for all mares ($P < 0 \cdot 01$) (Fig. 1). There was no significant difference

between the longevity of greys in the early and late years of the sample. Large factors of selection may well operate—at many periods grey horses appear to have been selectively exported and they show a high proportion of losses to the record. Most of the apparent reduction in their expectation of life is due to early deaths, the expectations at 10 and 15 years being 10·96 and 3·85 years in greys, as against 11·17 and 2·93 years in the whole of sample A. Causes of death are not given, and there is consequently no information about the incidence of melanomas, to which grey horses are sometimes subject (McFadyean, 1933).

Longevity of stallions

The Stud Book does not contain records of stallions comparable to those of mares. Three different estimates of thoroughbred stallion longevity have been obtained, with the help of other records—two are based (unlike the mare studies) on cross-sectional samples, and the third is a longitudinal study of the earliest age group for which a list of names could be had. All three leave a good deal to be desired, but they give some provisional indications of the rate at which the expectation of life declines with age in entire males.

Cross-sectional samples were taken of (a) all the animals listed in volumes 1 and 2 (1910 and 1913) and (b) all the animals listed in volume 5 (1921) of the Register of Thoroughbred Stallions (excluding the appendix). Thirty-three animals from sample (a) were still alive in 1921 and figure in both samples. The cohort sample was obtained by taking, from the lists of sires of brood mares in volumes 17 and 18 of the General Stud Book, all the stallions (180) foaled in 1880–84 inclusive. Life-tables were prepared by calculating age specific death rates from death and disposal records in the obituary and export lists of the Register, the General Stud Book, and the lists of premium stallions of the National Hunters and Light Horse Society.

Table V gives the full life-table for the two cross-sectional samples (correcting an error in the L_x column of the 1921 sample as originally published—Comfort, 1959*a*); and Table

Table V

ABBREVIATED LIFE-TABLES FOR THOROUGHBRED STALLIONS

	Listed 1910–1913					*Listed* 1921				
Age	n	q_x	L_x	e_x	σ_e	n	q_x	L_x	e_x	σ_e
4	9	0·0	1·0000	17·71	±0·84	2	0·0	1·0000	19·502	±0·75
5	38	·0526	1·0000			12	0·0	1·0000		
6	73	0·0	·9474			30	0·0	1·0000		
7	126·5	·0079	·9474			38·5	·0260	1·0000		
8	162	0·0	·9399			56	·0357	·9740		
9	195·5	·0102	·9399			63	0·0	·9392		
10	220	·0227	·9303	12·87	±0·58	81·5	0·0	·9392	15·6	±0·53
11	233·5	·0385	·9092			93	0·0	·9392		
12	240	·0208	·8742			111	0·0180	·9392		
13	244·5	·0123	·8560			112	·0268	·9223		
14	237·5	·0337	·8455			110·5	·0090	·8976		
15	217·5	·0276	·8170	9·31	±0·59	115·5	·0087	·8895	10·13	±0·50
16	201	·0199	·7945			110·5	0·0	·8817		
17	190·5	·0210	·7787			104	·0288	·8817		
18	176·5	·0453	·7623			97	·0619	·8563		
19	159·5	·0376	·7278			89	·0562	·8033		
20	146·5	·0956	·7004	5·41	±0·64	74·5	·0402	·7582	6·28	±0·47
21	122·5	·1061	·6334			58·5	·1026	·7277		
22	100	·1100	·5662			44	·0682	·6530		
23	71·5	·1399	·5039			35·5	·0282	·6085		
24	57	·1404	·4334			28·5	·1404	·5913		
25	43	·2093	·3726	3·01	±1·11	18·5	·2162	·5083	3·05	±0·52
26	27	·2222	·2946			10	·1000	·3984		
27	16·5	·2424	·2291			8	·2500	·3586		
28	11	·3636	·1736			6	·3333	·2690		
29	4	·2500	·1105			3	0·0	·1793		
30	2	0·0	·0829			2	1·0	·1793		
31	1	1·0	·0415					0·0		

VI gives the mean further expectation of life at 4, 10, 15, 20 and 25 years for all three samples of stallions, compared with the two main samples of mares. There is no significant difference at any age between the expectation of mares and of the

stallions in the cohort sample; the two cross-sections differ significantly from one another, from the mares, and from the cohort.

Table VI

EXPECTATION OF FURTHER LIFE (YEARS) FOR THOROUGHBRED MARES AND STALLIONS AT DIFFERENT AGES. (MEANS AND STANDARD ERRORS.)

	Stallions			*Mares*	
Age	*Listed* 1910 *and* 1913	*Listed* 1921	*Foaled* 1880–84	*Foaled* 1860–64	*Foaled* 1875–80
4	17·71 (0·84)	19·50 (0·75)	17·29 (0·72)	17·04 (0·21)	17·31 (0·21)
10	12·87 (0·58)	15·60 (0·53)	11·95 (0·73)	11·82 (0·21)	11·90 (0·20)
15	9·31 (0·59)	10·13 (0·50)	8·08 (0·69)	7·80 (0·20)	7·98 (0·20)
20	5·41 (0·64)	6·28 (0·47)	5·01 (0·67)	4·54 (0·22)	4·76 (0·21)
25	3·01 (1·11)	3·05 (0·52)	2·83 (0·43)	2·54 (0·45)	2·60 (0·35)

We can take our choice among these findings. The cohort sample is closest in date and method of treatment to the samples of mares, but it is small, and depends on only 38 conventionally "natural" deaths, none of them under 8 years of age, while of the two cross-sections, that for 1910–13 is probably the better, on grounds of size and absence of intervals in the middle of the table where $q_x = 0$.

Over most of the lifespan the plot of $\log q_x/t$ for both samples of mares is a presentable straight line with a doubling time of $3\frac{1}{2}$–4 years (see Sacher, this colloquium, p. 115). The present data are too poor for inference about its shape in stallions. Most of the apparent gain in male survival occurs over the years when mares may die of causes connected with foaling. The only valid conclusion from the figures is that contrary to the impression given by the uncorrected table (Comfort, 1959*b*), stallions are not shorter-lived than mares under these conditions of performance.

Conclusions

The main use of the study has been in providing a survival curve for a large mammal, sufficiently detailed to be used in criticizing hypotheses about lifespan determinants, for which maximum age-records are unsuitable. More such curves are badly needed. By the criteria needed in dealing with a matter as theoretically important as the supposed paternal age effect the study was too small and the chance of systematic biases, especially in losses, too large for convincing subdivision by parental ages, though the data were better than those on which such effects have sometimes been claimed. The literature of mammalian parental effects on longevity is contradictory, and has been reviewed elsewhere (Miner, 1954; Comfort, 1956). Yerushalmy (1939) found an increased stillbirth rate in babies with very old or very young fathers, but the difficulty arising from correlation between ages of spouses (Sonneborn, 1957) affects the value of such data. Our study was confined to parental age effects on longevity; paternal age has been held to affect other characters of stock performance, particularly by Russian breeders (e.g. Zamyatin *et al.*, 1946; Isupov, 1949; Ponomareva and Spitskaya, 1953; Pospelov, 1952; Eidrigevits and Polyakov, 1953; Barton, 1951; Frankland, 1955). Man and the horse, since they continue to breed into old age, are clearly the mammals in which such an effect on longevity is most likely to be demonstrable; our figures do not bear out the suggestion that old stallions have short-lived offspring, but it might still be desirable to examine the stillbirth rate in the mares which they covered. This, unfortunately, could not be done from stud-book records.

The small but positive correlation of filial with parental longevity is in accord with Beeton and Pearson's (1901) work, and with Haldane's (1949) interpretation of it—if heterozygosity is an important correlate of vigour, the sib-sib correlation of lifespan should be larger than that between generations. Perhaps the most striking feature of the study is the smallness

of the contribution, under these breeding conditions, made by short-lived parents to the next generation. There is, effectively, intensive spontaneous selection for longevity, which is not a deliberately-sought character in racehorses. Murie's work on sheep (1944) suggests that for some large mammals the wild adult survival curve is not very different from that in domestication. If this were true of wild horse populations, longevity of the dam, and probably, in the presence of competition between males, longevity of the stallion, would have a large selective advantage; the upper limit of the lifespan would have in this case to be fixed by something other than decline of selection pressure.

REFERENCES

BARTON, R. A. (1951). *Nature* (*Lond.*), **168,** 37.

BEETON, M., and PEARSON, K. (1901). *Biometrika*, **1,** 50.

COMFORT, A. (1956). The Biology of Senescence. London: Routledge.

COMFORT, A. (1958*a*). *J. Geront.*, **13,** 342.

COMFORT, A. (1958*b*). *Nature* (*Lond.*), **182,** 1531.

COMFORT, A. (1959*a*). *J. Geront.*, **14,** 9.

COMFORT, A. (1959*b*). *IV Int. Congr. Geront.*, **1,** 133.

EIDRIGEVITS, E. V., and POLYAKOV, E. V. (1953). *J. gen. Biol., Moscow*, **14,** 435.

FRANKLAND, H. M. T. (1955). *J. agric. Sci.*, **46,** 180.

HALDANE, J. B. S. (1949). *Ann. hum. Genet.*, **14,** 288.

IRWIN, J. O. (1949). *J. Hyg.* (*Lond.*), **47,** 188.

ISUPOV, A. P. (1949). *Horsebreeding, Mosk.*, No. 4, 29.

KADIĆ, M. (1949). *Jugosl. vet. Glasn.*, **2,** 602.

MCFADYEAN, J. (1933). *J. comp. Path.*, **46,** 186.

MATSUMOTO, K. (1935). *Z. Gestütk. Pferdez.*, **30,** 127, 165.

MINER, R. W. (ed.). (1954). *Ann. N.Y. Acad. Sci.*, **57,** 451.

MURIE, A. (1944). The Wolves of Mt. McKinley. Washington: U.S. Dept. Int. Nat. Parks Service.

PONOMAREVA, L. I., and SPITSKAYA, T. D. (1953). *Horsebreeding, Mosk.*, No. 23, 28.

POSPELOV, S. P. (1952). *J. gen. Biol., Moscow*, **13,** 445.

SCHOTTERER, A. (1939). *Dtsch. landw. Tierz.*, **43,** 228.

SONNEBORN, T. M. (1957). Proc. Ageing Conference, Gatlinburg. Washington, D.C.: A.I.B.S., in press.

VITT, V. O. (1949). *J. gen. Biol., Moscow*, **10,** 161.

WEBER, R. (1942). *Zool. Gart.* (*Düsseldorf*), **14,** 208.

YERUSHALMY, J. (1939). *Hum. Biol.*, **11,** 342.

ZAMYATIN, N., STOLBOVA, A., CHUGAEVA, M., and KUZNETSOVA, G. (1946). *Trud. Novosibirsk selskh. Inst.*, **7,** 107.

DISCUSSION

Rockstein: Perhaps the small but significant difference obtained for longer-lived animals from the older parents might have resulted because you started with a fairly long-lived strain, and you were dealing with inbred animals.

Comfort: This may be so; it has been said of at least one other strain of horses that the longevity depends on the proportion of English thoroughbred blood they have.

Rockstein: You said that among thoroughbreds there is a tendency to breed for longevity as well as for racing ability.

Comfort: This is not deliberate. It happens because short-lived animals contribute surprisingly little progeny to the total. Mares are not usually covered until they are taken out of training. As you know, horses in flat racing very rarely run over the age of four, whereas horses which are raced under National Hunt rules may go on being ridden up to quite high ages. Most of these animals here, if they had been raced, would have been raced before they were used as brood mares. The successful ones would then have been valued as brood mares; likewise the stallions—as soon as a stallion has made its name as a promising racehorse its value goes up enormously and it will be used to sire just as many foals as can be got out of it during the rest of its life.

Maynard Smith: I should like to make a few comments about the genetics of longevity. The consideration that was at the back of my mind in suggesting earlier that there might not be very much correlation between parents and offspring was as follows: if a character has been influenced by natural selection for a long time—if there has been natural selection tending to move it in one direction—then most of the genetic variability that is left will not be additive in the genetic sense, and will not give a positive correlation between father and child or mother and child, though it will, of course, do so between brother and sister. Resemblances of the kind that Prof. Jalavisto showed are very similar to the ones which I shall show you later on in *Drosophila*; that is, there are resemblances between parents and offspring of the same sex, but not of different sexes. This pattern is what one would call sex-limited, and would be expected if the causes of death were to some extent different in the two sexes. On the other hand, if you get a resemblance between mother and son, and father and daughter, as you might in some cases, then this is what would be expected in sex-linked inheritance.

Comfort: I do not think one can get much along those lines out of my data. The differences for the two sexes scored separately was very small. The subjects were all fillies, but you have to score both parents to get a significant difference.

Hartwig: Have you also studied the influence of parental age on the fertility of the offspring ?

Comfort: No. I could probably do so now, by going through the data again. But it would mean following each life from start to finish and counting the number of foals. In many instances there is some doubt whether the animal missed or whether it miscarried. The Stud Book usually distinguishes cases where the foal was born dead, or where there was a miscarriage, from those where the mare failed to conceive; but one would have to be sure of differentiating between unsuccessful pregnancies, and pregnancies which did not take place at all. The other trouble is that as the animals are not crossed twice with the same stallion in succession, one would have to allow for the fertility of the stallion, which varies a great deal. In these thoroughbreds there is a surprisingly high rate of infertility.

Kershaw: You showed a death curve [not printed] which starts with a slow rise on the left. The figures which we had on industrial horses, that is draught horses and police horses, show that while the general survival curve is the same, the death curve may have its slow fall on the right (Chalmers, T. A., Kershaw, W. E., and King, J. O. L. (1956). *Nature* (*Lond.*), **178**, 48). I assume that the arbitrary end-point in the racehorses is in part economic; in those figures of ours for the draught horses and the police horses it was certainly economic. This suggests that the curve of death is arbitrarily determined by the index that one uses. We had assumed that the working life had some relation to natural longevity. It does seem now, in animals for which one can get the same data for different indices, that the different indices may produce curves which are made up differently.

Comfort: What was the maximum age for the police horses ?

Kershaw: Fifteen to twenty years.

Comfort: These thoroughbred mares live a good deal longer. My figures refer to breeding practice during the last century. The maximum age is lower today, particularly in mares from commercial studs, which are put out at 23–24 years, but rather less so in stallions. The number of stallions which "fall dead" and the number of them recorded as having died of old age is large, even now. They are kept, if they were famous animals, very much as pets of the establishment. One of the common, and I suppose the most enviable, terminal entries, is "fell dead after serving a mare".

LIFESPAN OF CATTLE AND HORSES UNDER VARIOUS CLIMATIC CONDITIONS AND THE REASONS FOR PREMATURE CULLING

W. Hartwig

Institut für Tierzucht, Martin-Luther-Universität, Halle

In cattle breeding performance can be separated into two major components: (1) the special productivity (of milk, meat, wool), (2) the general performance. General performance means: fecundity, longevity, power of resistance to disease (particularly to those hereditary diseases caused by failure to adapt to environmental changes), food utilization and so on. Certain factors of the general performance, including longevity, also come under our definition of constitution. Besides the increase in special performance, the improvement of the general performance of agricultural domestic animals is a primary object of cattle breeding; in particular increased lifespan must be considered.

In the determination of the real duration of life of large agricultural domestic animals there are, however, considerable difficulties. First of all domestic animals are kept for their economic productivity; their lifespan is therefore affected by economic considerations and is more or less variable. Factors such as decreased performance, hard milking, price relations between milk and meat, shortage of space, period of feeding, bad fodder in some years, technical developments, etc., may lead to the sale for slaughter of completely healthy animals that could have lived longer. That is why, in considering the average age of living animals, we have to deal not with a real biological parameter, as in human vital statistics, but with arbitrarily biased values. Other conditions are to be found,

however, where exterior circumstances are not controlled directly by man (for instance, diseases, epidemics, inferior constitution and its consequences, all influence the lifespan of animals). Here we get approximate real values of the lifespan, man and animals in their struggle with nature being exposed to these influences everywhere.

The major task in cattle breeding and veterinary science is to analyse the struggle against the various factors which shorten the age of productive animals and contribute to their premature culling. In the following discussion of the age of cattle and horses first of all the average age of living animals and then the recorded average age of herd-book animals of various species will be given. Finally the most important reasons influencing the premature culling of animals will be considered. The lifespan of cattle has been examined in detail in recent years, but there are still only a few results regarding horses. This fact is easily comprehensible because cattle breeding is of great economic importance in many countries, while the importance of the horse has diminished considerably as a result of increased mechanization.

Milch cows

The research listed in Table I covers about 25 years, from 1932 to 1957. It will be noted that cattle of highland breeds show a longer lifespan, 1–1·7 years on an average, than lowland cattle. It is not possible to explain clearly how far this difference is based on breed-conditioned, genetic factors and how far it may be attributed to climatic circumstances, quality of soil or economic reasons. The average lifespan of the different breeds is between 4·7 and 9·35 years and the general average age is 7·1 years. Three years may be subtracted for breeding and the productive period therefore amounts to 1·7 to 6·3 years. It is a fact proved by many authors that the productivity of the animals rises according to the number of lactations after the fifth to the seventh calf;

that is to say the highest productivity is reached between 7 and 9 years, depending on the breed and the individual animal, and then it decreases again gradually. This optimal age of productivity is not attained by the average animal.

Table I

AVERAGE AGE OF LIVING COWS OF VARIOUS BREEDS

Breed	*Author*	*Number of cows examined*	*Average age (yrs.)*
Lowland cattle			
Scottish cows	Wright (1933)	—	6·4
English breeds	Smith, Buchanan and Robinson (1932)	— (milk-fattened)	5·5–6·0
American breeds and Iowa	Cannon and Hansen (1940)	—	4·7
Black-pied Schleswig-Holstein	Ripke (1938)	4,000	7·4
Black-pied, East Prussia	Bauer (1940)	—	6·2
Black-pied and red-pied (Rhineland)	Mannes (1947)	4,000	6·81
Black-pied (Rhineland)	Schieren (1948)	4,000	8·1
Various breeds (North-western Germany)	Winnigstedt (1949)	—	6·4–7·1
Unicoloured red cattle	Winnigstedt (1949)	—	7·2
Shorthorn	Winnigstedt (1949)	—	6·6
Anglia cattle	Ziegenhagen (1951)	—	6–7
Red-pied lowland cattle (Minsterland)	Röttgermann (1953) 1910–1950 controlled cows	—	5·6–7·0
Black-pied coloured cattle (Saxony-Anhalt)	Hartmann (1953)	1,455	7·4
Highland cattle			
Swiss brown cattle	Engeler (1947)	4,361	8·5
Spotted cattle (Simmental)	Stockklausner (1937)	30,000	6·5–7·6
Spotted cattle (Bavaria)	Hagel (1939)	3,000	9·0
Brown cattle (Wurtemberg)	Piel and Rumbaur (1948)	—	9·35
Spotted cattle (Upper Bavaria)	Martin (1950)	2,150	9·23
Spotted cattle (Northern Baden)	Wurzel (1952)	166	7·11

It is easy to see that the average productivity of many cows would be considerably higher if they lived to a greater age. This alarming circumstance has been pointed out repeatedly in recent years. We cannot, however, fully agree with the

opinion sometimes expressed, that the age of the animals would decrease as a consequence of higher productivity. Mannes (1947) and Dietrich (1956) succeeded in proving, in the course of their researches on red-pied coloured cows in the Rhineland and on black-pied cows in Saxony, that long-lived cows produce more milk, even during their earlier years, than those having a short period of produce, and that highly productive cows live to the greatest age. From the results shown below it can be seen that there has been a general rise in the average lifespan of herd-book animals, even though the productivity has also risen considerably.

Table II

Average age of black-pied cattle of the Middle-Weser association of cattle breeders (from Böttcher, 1952)

Date	*No. of cows*	*Average lifespan (yrs.)*
1930	420	5·5
1935	752	6·0
1940	1,094	5·9
1945	1,618	6·5
1949	1,722	6·9

The rise in the average age in 20 years was 1·4 years. Ziegenhagen undertook the same examination of the Anglia breed (Table III).

Table III

Average age of Anglia cattle (from Ziegenhagen, 1951)

Date	*No. of cows*	*Average lifespan Yrs. Mos.*
	A: Herd-book cows	
1924	9,851	5 10
1929	9,458	6 10
1932	7,797	7 2
1939	8,492	7 10
1947	9,831	7 11
	B: Herd-book and not herd-book	
1930	15,830	6 1
1939	14,991	6 1
1947	29,350	6 7

The rise in average age of herd-book cows of this breed therefore amounts to 2 years, 1 month, and cattle not registered in herd-books showed the same tendency.

Finally, let us mention the values for grey-brown highland cattle (Table IV).

Table IV

AVERAGE AGE OF GREY-BROWN HIGHLAND CATTLE (HERD-BOOK)

Date	*Average age* *Yrs.*	*Mos.*
1900	5	8
1925	6	11
1949	7	3

Like the lowland cattle they show an increase in age, amounting in this case to 1 year, 5 months. This generally observed tendency to an increase in age is due to improved feeding, to improved methods of keeping and breeding and to the struggle against epidemics and disease.

Besides the age of living cattle, the age of cattle at death is of great interest, for this gives a clear idea of the average longest lifespan of the animals. In this case it does not matter whether the animals were killed because of insufficient productivity or whether they died as a result of epidemics, disease or accident. Böttcher (1952) gives the figures shown in Table V.

Table V

AVERAGE AGE AT DEATH OF BLACK-PIED CATTLE OF THE MIDDLE-WESER BREED (BÖTTCHER, 1952)

Date	*No. of cows*	*Age (yrs.)*
1930	559	6·4
1935	1,482	7·2
1940	2,205	7·2
1945	3,171	7·9
1949	2,665	8·2

Table VI gives results found by König (1951) for another breed.

In both these studies on the age of cows at death we find the same trend as in the ages of living animals already quoted. Although there is a rise in age at death, it still remains true that the majority are culled before they reach the years of greatest productivity.

Table VI

Average age at death of grey-brown highland cattle (herd-book) (König, 1951)

Date	*Yrs.*	*Mos.*
1901	6	9
1925	8	4
1949	9	4

Röttgermann (1953) has carried out research on the age structure of red-pied cows in Westphalia and the Rhineland. From 1944 to 1951 an average of 36 per cent of cows were aged up to 5 years, 51 per cent were aged from 5 to 10 years, and only about 13 per cent were older than 10 years. Thus 87 per cent of cattle died before attaining their tenth year.

Freudenberg and Francke (1956) found that in black-pied cattle of the Central-German arid region the highest number of deaths occurred between the fourth and the eighth years. At the age of 3, 14·7 per cent of the cattle died; at the age of 5, 21·3 per cent; at 6, 22·6 per cent; at 7, 13·2 per cent; and at the age of 8, 9·8 per cent. Thus 81 per cent of all the cows died in these five years, and the average age at death was 6·43 years. This ratio of losses is high, considering that these figures are for herd-book cattle which are valuable for breeding and might be expected to be kept alive longer. The figures for cattle not registered in herd-books reveal still worse results.

In this connexion we need to ask what are the causes that have a decisive influence on the age of the animals and lead to their premature culling or death. Freudenberg and Francke (1956) performed special researches along this line on 469 cows from 12 big farms of the arid Central-German district. They found the following reasons for suppression. First, 54·8

per cent of the animals were sterile; the authors pointed out that this is due to genital tuberculosis as well as to Bang's disease, which causes most of the sterility. Secondly, 12·79 per cent of them had tuberculosis (udder tuberculosis included). Thirdly, inflammation of the udder accounted for 7·89 per cent. The remaining 115 animals died from various other diseases, such as cancer of the lungs and cardiac weakness.

Dinkhauser's (1940) investigations in Lower Saxony showed that 23 per cent of all cattle had to be culled because of sterility. From research in the Central-German dry region Marlow (1951) succeeded in showing that softening of the bone was the most important cause of death. In his researches on cattle from smaller farms in Baden, Gerner (1952) obtained the following results:

1.	Sterility	32·0 per cent
2.	Tuberculosis	14·2 ,, ,,
3.	Swallowing foreign bodies	13·4 ,, ,,
4.	Other diseases	13·0 ,, ,,
5.	Age	21·0 ,, ,,
6.	Insufficient productivity	6·1 ,, ,,

Other diseases here means those that are specially connected with the sexual organs, such as dropping of the womb and emergency slaughtering at calving. Piel and Rumbaur (1948) studied the causes of death in first-class brown cattle in Wurtemberg. They obtained the following results:

1.	Sterility	24·3 per cent
2.	Tuberculosis	4·6 ,, ,,
3.	Brucellosis	1·7 ,, ,,
4.	Age	23·4 ,, ,,
5.	Slaughtering without indication of cause	26·0 ,, ,,
6.	Garget	11·7 ,, ,,
7.	Foot-and-mouth disease	2·9 ,, ,,
8.	Emergency slaughtering	5·4 ,, ,,

From research into the family history tuberculosis was found in 41 families, six of which had two or more cases. The authors therefore suppose that there is a hereditary inclination to tuberculosis, as the same phenomenon is to be found in human medicine.

Martin (1950) performed research on this line on 2,160 cows in Baden. Piel (1951) examined the reasons for culling 2,507 brown Wurtemberg cattle from 1939 to 1944, while Ziegenhagen (1951) examined the causes of death of 5,244 Anglia cows. These authors found that the causes were more or less the same as described above. All these statements clearly demonstrate that sterility, tuberculosis, garget, brucellosis and softening of the bones are the most important diseases and deficiencies that lead to culling of breeding animals and shorten their lifespans and utilization as brood cattle.

Using black-pied cows of various ages from the Central-German dry region, Spohde (1948) undertook research on death from the three most important diseases (sterility, tuberculosis and garget). Of all the cows culled because of sterility, 78 per cent were aged from 4 to 8 years. Sixty-eight per cent of tuberculous animals were culled between the ages of 5 and 7 years; 78 per cent of the animals infected with garget were also culled at these ages. These three principal diseases cause the relatively premature suppression of animals in the second to fifth years of life, that is to say at an age when their maximum capacity has not yet been reached.

The different measures that might be taken in order to raise the average age of the animals include breeding, by scrupulous selection, for fecundity, longevity, and intensified resistance to diseases, with simultaneous stress on optimal productivity, as well as improvements in breeding, keeping and feeding.

Bulls

In his studies on the ages of bulls in Brunswick slaughterhouses Hogreve (1955) found the following average ages: bulls from the South Hanover–Brunswick region, 3 years, 5 months;

from Lüneberg, 3 years, 4 months; from East Friesland, 3 years, 4 months. He concludes from this low age of death that the premature culling of bulls is due more to private and economic reasons than to the proper physiological limit of productivity of the individual animals. Hartwig (1959, unpublished) examined the average age at death of 2,000 herdbook bulls from Saxony-Anhalt. An average age of 4 years, 9 months was noted; 83·5 per cent of the animals had been killed because they were no longer used for covering. The reasons for this were principally economic, as Hogreve had also found. Schröder (1958) found a higher average age of 5 years, 4 months among suppressed bulls kept for fertilization. In insemination stations we find that the bulls are kept by means of better utilization of breed and better conditions so that the animals in general grow older. Schröder found 19 bulls which were older than 10 years. The most important causes of death of the bulls were:

culled for genetic reasons	60 bulls	=	20·27 per cent
diseases of the genital system	59 ,,	=	19·9 ,, ,,
tuberculosis	58 ,,	=	19·5 ,, ,,
diseases of the legs	33 ,,	=	11·1 ,, ,,

Five per cent of the bulls were slaughtered after swallowing foreign bodies and 2 per cent because of viciousness. Here again economic aspects play the leading part, so that these factors make the determination of a real average age impossible. Cows and bulls can both reach 18 or 20 years of age, though these figures are exceptional.

Horses

It is very difficult to make corresponding observations on the regional breeding of horses, therefore these studies were carried out on stallions that were kept as long as they continued to breed. For that reason a better estimate of their real age at death can be made. Research along this line has been undertaken on stallions in the district stud of Kreuz by

Wussow and Hartwig (1956–57). All of the 635 stallions were examined carefully and classified according to breed in order to find the average age of each breed. The following values were noted:

	Average age (yrs.)
20 East Prussian stallions	15·3
24 Hanoverian	13·6
52 Oldenburg	12·9

The average lifespan of warm-blooded* stallions was 13·8 years.

	Average age (yrs.)
150 original Belgian and Dutch stallions	13·2
53 stallions of the Rhineland	12·6
42 imported English cold-blooded stallions	10·5
284 Belgian stallions, born in Saxony	10·4

The average lifespan of cold-blooded* stallions was 11·5 years.

Table VII gives a summary of the ages at death of different breeds. This table shows that well-bred or thoroughbred warm-blooded horses have the longest lifespans. They also have the highest percentage of stallions reaching an age of more than 15 or 20 years, whereas by the age of 15, 81 per cent of the cold-blooded horses have died and only 0·7 per cent reach an age over 20 years. Oldenburg stallions, being heavy but warm-blooded, show a lifespan that is between the well-bred warm-blooded and the cold-blooded horses. From the above it seems that thoroughbred and well-bred warm-blooded horses have a better constitution and live to a greater age than do cold-blooded ones. The constitution of the animals seems less good the less thoroughbred blood they have. This tendency can also be found in examining the lifespan of mares. Flade (1958), for instance, while doing research on 64 Arab thoroughbred mares born between 1921 and 1945 in Poland, found an

* "Warm-blooded" horses are thoroughbreds; "cold-blooded" horses are heavy ones.

Table VII

AGES OF STALLIONS AT DEATH

53 thoroughbred and well-bred warm-blooded horses:

Age group	*No. of stallions*	*Percentage*
3– 5	5	9·5
3–10	22	40·6
3–15	31	58·5
3–20	42	79·0
	10 stallions attained an age over 20 years =	19·0

52 heavy warm-blooded horses (Oldenburg and Friesian):

Age group	*No. of stallions*	*Percentage*
3– 5	9	16·0
3–10	21	40·3
3–15	34	63·3
3–20	50	96·0
	2 stallions reached an age of more than 20 years =	4·0

534 cold-blooded horses:

Age group	*No. of stallions*	*Percentage*
3– 5	63	11·8
3–10	229	42·9
3–15	434	81·0
3–20	530	99·3
	4 stallions reached an age of more than 20 years =	0·7

average age of 16·7 years. Konopinski and Detkens (quoted by Flade) found an average age of 11·5 years for 598 half-bred Poznan mares in Poland.

The most important causes of the premature culling of stallions are, according to Wussow and Hartwig (1956–57), the diseases and constitutional faults shown in the table on p. 68, which were observed in 390 stallions whose causes of death were evident.

In summary we can state the following points concerning the average lifespan of cattle and horses:

1. Research on living cows of 19 different breeds revealed an average lifespan of 7·1 years (4·7–9·35 years). This average is undesirably low, because the majority of the animals are culled before attaining the years of highest productivity.

2. Research on various breeds shows a small rise (1·5 to 2 years) in the average lifespan both of living cows and of cows which died during the past two or three decades. We cannot agree with the often expressed opinion that increased productivity will cause the premature death of the animals.

	Stallions	*Percentage*
1. Colic	135	34·0
2. Dermatitis verrucosa (malanders)	74	19·5
3. Disease of the heart, lungs and chest	58	15·1
4. Bad covering	52	13·5
5. Weakness of the legs	30	8·0
6. Sepsis	12	3·1
7. Viciousness	11	2·8
8. Sleepy staggers (Borna)	9	2·3
9. Cancer	8	1·8
Total	390	100·0

3. The lifespan of cows is considerably influenced by economic factors, which frequently lead to the premature killing of healthy animals.

4. The most important causes of death that have a great influence on the lifespan of cows are sterility, tuberculosis and garget (mastitis).

5. The average lifespan of bulls is still lower. Economic factors act even more intensively here, so that the animals only attain an average lifespan of between 3 years, 5 months and 5 years, 4 months.

6. The average lifespan of Arab mares in Poland was stated to be 16·7 years and that of Poznan half-bred mares 11·5 years.

7. Warm-blooded stallions at the Kreuz stud attained an age of 13·5 years and cold-blooded stallions of Belgian origin 11·5 years.

8. The lifespan of horses seems to decrease the less they are related to English and Arab thoroughbreds.

9. The most important causes of loss of the stallions were: colic, dermatitis verrucosa (malanders), infirmity of the heart, chest and lungs, and bad covering.

REFERENCES

BAUER, K. (1940). *Z. Tierz. ZüchtBiol.*, **47**, 261.
BÖTTCHER, T. (1952). Völkerode, Sonderdruck, 18.
CANNON, C., and HANSEN, E. (1940). *Züchtungskunde*, **15**, 193.
DIETRICH, H. (1956). Dissertation, Halle.
DINKHAUSER, F. (1940). *Dtsch. landw. Tierz.*, **44**, 153.
ENGELER, W. (1947). Das schweizerische Braunvieh.
FLADE, J. E. (1958). *Arch. Tierz.*, **1**, 354.
FREUDENBERG, F., and FRANKE, G. (1956). *Dtsch. Landw., Berl.*, **7**, 301.
GERNER, K. (1952). *Tierzüchter*, **4**, 589.
HAGEL, L. (1939). Dissertation, Munich.
HARTMANN, W. (1953). Dissertation, Halle.
HARTWIG, W. (1959). Unpublished results.
HOGREVE, F. (1955). *Tierzüchter*, **7**, 60.
KÖNIG, K. (1951). Allgäu. Bauernblatt.
KONOPINSKI and DETKENS (quoted by Flade, 1958).
MANNES, A. (1947). Dissertation, Hannover.
MARLOW, H. (1951). Dissertation, Halle.
MARTIN, W. (1950). *Züchtungskunde*, **22**, 97.
PIEL, H. (1951). *Züchtungskunde*, **23**, 79.
PIEL, H., and RUMBAUR. (1948). Dissertation, Hohnheim.
RIPKE, G. (1938). Dissertation, Munich.
RÖTTGERMANN, W. (1953). *Z. Tierz. ZüchtBiol.*, **62**, 1.
SCHIEREN, J. (1948). *Dtsch. tierärztl. Wschr.*, **55**, 49.
SCHRÖDER, G. (1958). Thesis, Halle.
SMITH, BUCHANAN, A. D., and ROBINSON, O. J. (1932). *Z. Tierz. ZüchtBiol.*, **25**, 307.
SPOHDE, H. (1948). Thesis, Halle.
STOCKKLAUSNER, F. (1937). *Dtsch. landw. Tierz.*, **41**, 570.
WINNIGSTEDT, R. (1949). *Züchtungskunde*, **20**, 193.
WRIGHT, N. C. (1933). *Züchtungskunde*, **8**, 424.
WURZEL, W. (1952). *Züchtungskunde*, **23**, 239.
WUSSOW, W., and HARTWIG, (1956/57). *Wiss. Z. Martin-Luther-Univ.*, **6**, 13.
ZIEGENHAGEN, G. (1951). *Z. Tierz. ZüchtBiol.*, **59**, 331.

DISCUSSION

Benjamin: The improvement in average lifespan in the more recent groups you mentioned was very much smaller than in the cattle in earlier years. Is there some sort of resistance to increasing the lifespan or is there some other factor involved ?

Hartwig: The overall tendency was towards an increased lifespan, and the smaller increment there is not significant.

Bourlière: Is there any correlation between the average lifespan of the different breeds of cows and their weight ?

Hartwig: The lighter cattle live longer than the heavy ones.

Danielli: Have you any data for highland cattle living in the lowlands, and *vice versa* ?

Hartwig: There is the example that when cows were exported to Africa the highland cows adapted themselves better to those conditions than the lowland ones.

Kershaw: When were these cattle exported ?

Hartwig: At the end of the 1920's.

Kershaw: In that case there is a complicating factor, because I have seen their progeny in the Cameroons and they are remarkably resistant to sleeping sickness.

Danielli: To what extent is this increase in average age due to better veterinary services?

Hartwig: That is too complex to answer and I am unable to decide the cause of it.

Danielli: Unless one has some idea of the extent to which some specific disorders have been suppressed by veterinary work, it is very difficult to evaluate the data at all.

Hartwig: The veterinarians claim that they helped towards this increase, but on the other hand the breeders say it is due to their work.

Comfort: Has it been possible, in your data on horses, to compute lifespans or life-tables in the same sort of way as I have done, on the basis of age-specific natural death rates allowing for the animals lost or culled ?

Hartwig: Yes, that has been done.

Comfort: The agricultural lifespans are a very different matter indeed from those of horses, which are kept to advanced ages. I am sure these cows would live a great deal longer if they were not culled.

Hartwig: I agree with you.

Comfort: It would be very useful if we could get a good life-table for one of the heavy breeds for comparison with thoroughbreds.

Hartwig: The great difficulty is that if these animals are not kept for breeding purposes they are mostly sold and records are very difficult to obtain.

Mühlbock: Cancer research workers are very interested in keeping cattle to the end of their lives, because no one has ever seen a mammary tumour in cattle. The question is are they naturally resistant, or are they slaughtered before they reach the age at which tumours would develop? A considerable amount of money is now being collected just to keep cattle to the end of their natural lives to see what happens.

There is another cancer in cattle which is very peculiar, and that is the so-called "cancer eye", or cancer of the conjunctiva. It is a very interesting condition, hardly ever seen in Europe, but more often found in countries with plenty of sunshine. It is thought to be a virus infection, and studies are being carried out in Texas where a great number of cattle are kept just for this purpose. Gerontologists could therefore find out from this material what the normal lifespan is.

Wolstenholme: Could one obtain any figures from the cattle in India, which are allowed to live their normal lives to the full?

Comfort: There is an institute in India which studies these cattle, but their ages are not known, and unless one has reliable stud-book records and the actual date of the calving it is no good. If I was unjustifiably sceptical about centenarians who have birth certificates, I would be ten times more sceptical about a sacred cow which has not.

Wolstenholme: Have any sacred cows been seen to have mammary tumours?

Mühlbock: They are in such a poor condition that it is no wonder that they do not get any.

ONSET OF DISEASE AND THE LONGEVITY OF RAT AND MAN

HENRY S. SIMMS, BENJAMIN N. BERG, and DEAN F. DAVIES

Department of Pathology, College of Physicians and Surgeons, Columbia University, New York

IT is self-evident that the longevity of any species, such as the rat or man, depends upon the age range at which the major diseases of that species result in death. This, in turn, depends upon three factors:

First, the ages at which early lesions of the major diseases are most likely to appear in individuals of the species. (This we call the "probable age of onset.")

Second, the time required for lesions to develop from the early stages to the severe lesions that cause death.

Third, the effect of advancing age on the onset of lesions in that species.

The combined action of these three factors results in the mortality curves with which we are familiar (Fig. 1).

One hundred and thirty-four years ago Gompertz (1825) published his law relating mortality with age. More than one hundred years later this law was rediscovered by one of the present authors—and this started him on a career in gerontology. The law may be expressed in the following form:

$$\text{Log } P_{\text{M}} - \text{Log } P_{\text{MO}} = k_{\text{M}}t$$

where P_{M} is the probability of death (mortality rate) at age t, P_{MO} is the (extrapolated) probability of death at the age of birth, and k_{M} is a constant having a positive value.

Fig. 1 shows a plot of the logarithm of mortality rate against age. This is seen to be approximately a straight line throughout adult life. The equation of this line is the one just given.

For nearly 15 years we have been studying the onset of lesions in rats in relation to age and longevity. For the purpose of these studies we established a special rat colony with conditions that were unusually favourable and uniform. The temperature was kept constant (76° F). The humidity was kept at about 60 per cent. The lighting was indirect and

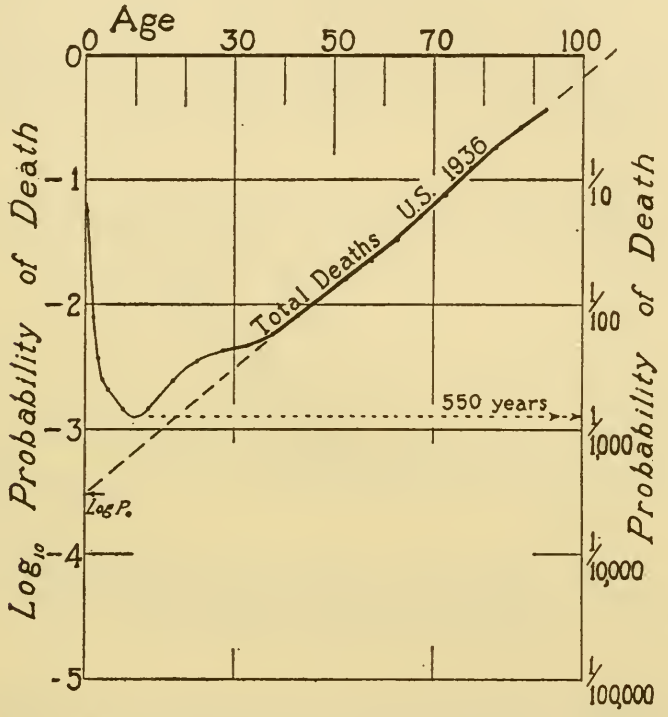


FIG. 1. Logarithm of human mortality, plotted against age (From Simms, 1946).

Figs. 1–5 reproduced by courtesy of the Editor, *Journal of Gerontology*.

was the same in all cages, with 12 hours of light and 12 hours darkness each day throughout the year. The diet was uniform and the quarters were quiet and clean. Data on growth and disease in rats kept under these conditions have been reported by Berg and Harmison (1957).

Finally, we were able to reduce respiratory infection (and other infections) to such a low level that they were practically non-existent. Under these conditions it was possible to study

the onset of lesions (of a non-infectious nature) in relation to age and in relation to mortality and longevity.

Fig. 2 shows the percentage of male rats that showed detectable lesions of five selected diseases (Simms and Berg, 1957). Each curve is an S-shaped curve approaching a maximum level of incidence. Two of these curves approach 100 per cent, whereas the other three approach lower levels of incidence.

It will be noted that the curve for chronic nephrosis and glomerulonephritis and also the curve for myocardial degeneration are spread over a wide age range. This means that onset

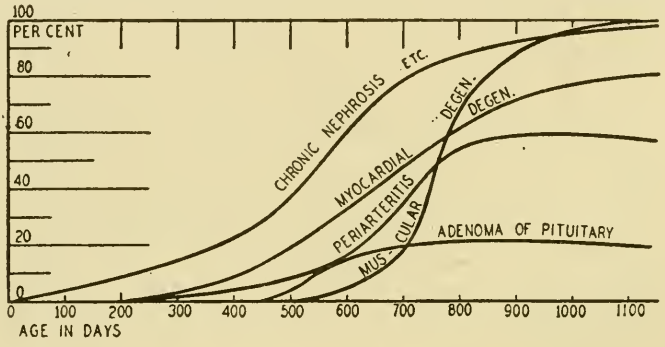


Fig. 2. Percentage of rats having detectable lesions of five major diseases, plotted against age at autopsy (From Simms and Berg, 1957).

of these lesions was observed in some rats at an early age but in other rats it was not seen until they were much older. On the other hand, onset of muscular degeneration occurred in all rats within a narrow age range (lasting only about 500 days). In the majority of the rats the onset of detectable lesions of this disease occurred between 700 and 900 days of age. Hence our rat colony was quite homogeneous in regard to this disease—but much less homogeneous in regard to other diseases.

Fig. 3 shows the slope of these curves at various ages. Each curve in this chart represents the *age* distribution *of onset* of a disease. For example, muscular degeneration (Berg, 1956) had

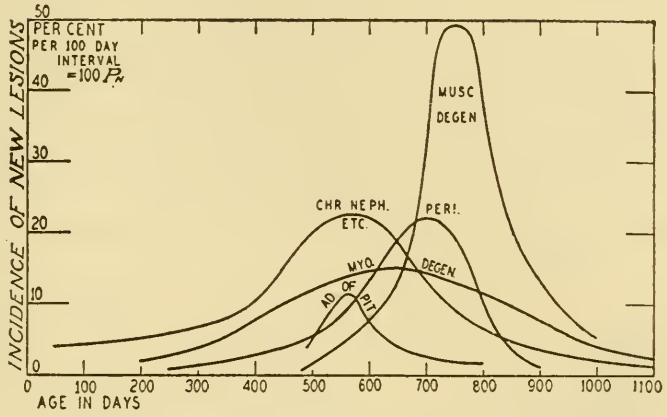


FIG. 3. Age distribution of onset of rat lesions. These curves show the probability of onset at various ages (among the total number living at each age) (From Simms and Berg, 1957).

its greatest probability of onset at 750 days of age, although a few rats acquired lesions at 500 days—and some not until 1,000 days. Similarly, the peak for chronic nephrosis and glomerulonephritis was 580 days and the peak for periarteritis was 710 days.

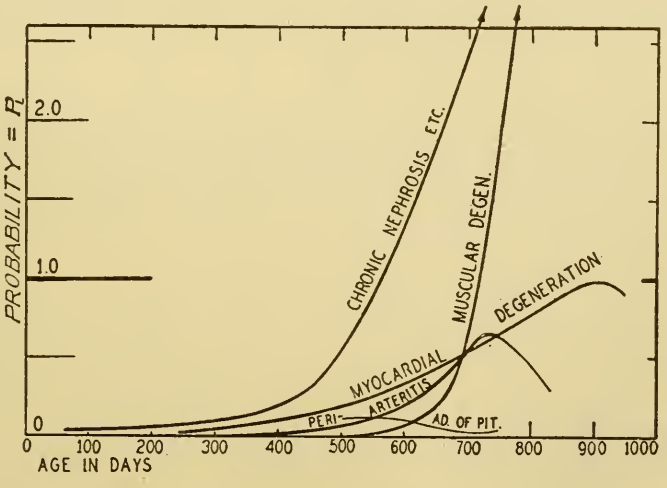


FIG. 4. Probability of onset of new lesions among the surviving rats having no lesions (From Simms and Berg, 1957).

The reason why the curves fall off after reaching a maximum is simply that there are fewer remaining animals without lesions of a given disease and which consequently can acquire lesions for the first time. There is no decrease in the tendency to form lesions among those individuals that have survived to advanced age without them. This is shown in Fig. 4, where it is seen that the tendency to form lesions increases progressively with age.

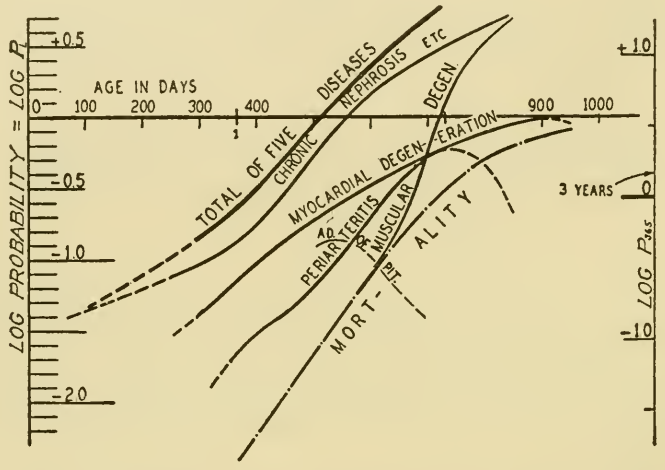


Fig. 5. Logarithm of the probability of onset of new lesions (among surviving rats having no lesions). Also a curve for rat mortality (From Simms and Berg, 1957).

That this increase is a logarithmic function of age is shown in Fig. 5, where the *logarithm* of the probability of onset (among rats not having lesions) is plotted against age. These curves approximate to straight lines. Note that they parallel the bottom curve for mortality of rats.

We may now compare rat and man. Fig. 6 contains two charts each having data from both rat and man. At the left end of the top chart are curves for occurrence of lesions in rats. These are identical with the curves in Fig. 2, except that here the time scale is very much condensed, making the curves much steeper. Similarly, at the left end of the bottom chart are curves for the distribution of onset of lesions in

rats. These are identical with those in Fig. 3, except that the time scale is here very much condensed.

At the right-hand end of these charts are data on man—plotted on the same time scale as the rat data. These data were obtained by one of us (Dr. Davies) in 1945–46 while working in this department. Examination was made of over 500

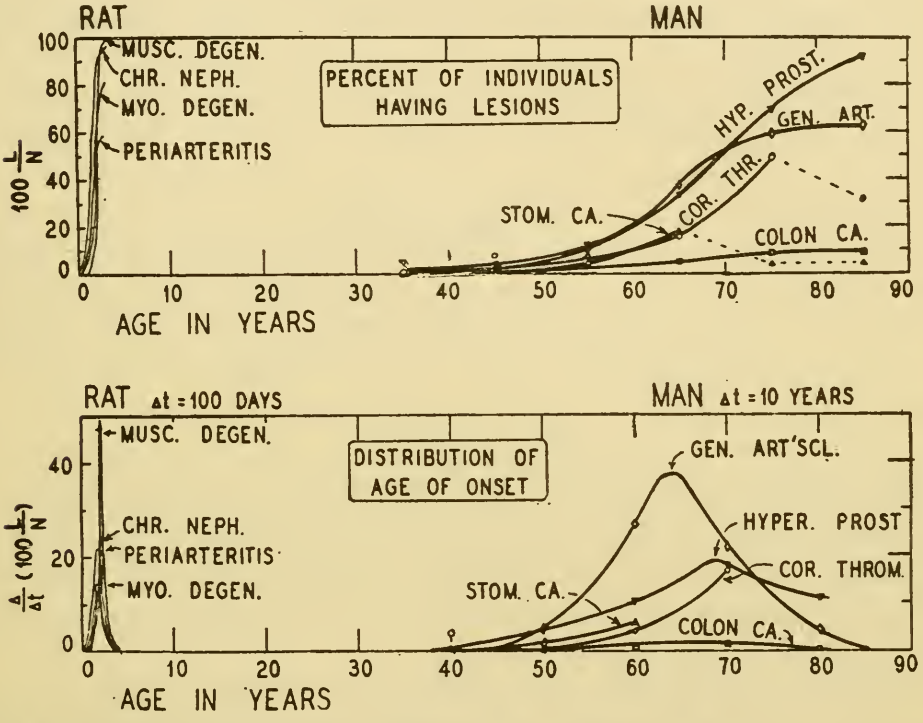


FIG. 6. Data of rat and man plotted on the same age scale.
Top Chart: Percentage of individuals having detectable lesions of diseases of their species.
Bottom chart: Age distribution of onset of lesions (probability of onset).

autopsy records of the Presbyterian Hospital. The data were tabulated and some of the findings on males are reported here. We recognize that such data are open to the criticism that the autopsies were performed by numerous pathologists and that the cases came from a very heterogeneous population. However, these objections apply equally to all the age groups reported. Unfortunately, the number of cases in the upper

age groups was small (56 males in the 70–79 group and 12 males in the 80–89 group).

It will be seen from Fig. 6 that when the data of rat and man are plotted on the *same time scale*, the curves of the two species are identical in form, except that those of the rat occur much sooner, and are compressed into a much shorter time range, than those of man. This applies not only to one or two diseases of each species, but also to other diseases not reported here.

It should be pointed out that the rat data were obtained from a fairly homogeneous colony of animals raised under uniform conditions. On the other hand, the human data were obtained from a heterogeneous collection of individuals who had lived under differing conditions. Had the humans been as homogeneous as the rats, their data on these two charts would be characterized by much steeper curves within a much narrower time range—perhaps approximating to the curves of the rats in shape, but not in their location on these charts.

Hence, we may conclude that the factors which determine the longevity of these two species (rat and man) appear to be identical, except that in one species the lesions of the major diseases have their onset much sooner and over a much shorter range of time, than do those of the other species, when compared on the same time scale.

That it is possible to alter the age of onset of lesions has been shown by dietary experiments in which rats on a restricted food intake were found to have a considerable delay in the onset of their major diseases, as compared with rats receiving as much food as they wanted to eat. This suggests that there may be other methods for modifying lifespan which may result in altering the age of onset of lesions of major diseases.

Summary

Observations on the accumulation of lesions in rats in relation to age have shown that the lifespan of these animals

is directly related to the age of onset of lesions of the major diseases of this species. The age of onset of these lesions, when plotted against age, gives smooth curves which are characteristic of the diseases in question.

Data on human lesions, found from autopsy data at different ages, give curves similar to those of rats, except that the onset of the human diseases does not occur until many years later than is the case with the rats. This indicates that there is a mechanism for the deferment of onset of lesions, which accounts for the difference in lifespan between the species.

REFERENCES

Berg, B. N. (1956). *J. Geront.*, **11**, 134.
Berg, B. N., and Harmison, C. R. (1957). *J. Geront.*, **12**, 370.
Gompertz, E. (1825). *Phil. Trans.*, **115**, 513.
Simms, H. S. (1946). *J. Geront.*, **1**, 13.
Simms, H. S., and Berg, B. N. (1957). *J. Geront.*, **12**, 244.

DISCUSSION

Gerking: The curve showing the age distribution of onset of disease in your rats was a normal, or nearly normal distribution. The right-hand portion of the curve of deaths that Dr. Benjamin showed us, indicating senescence in the human, was also the normal distribution. These both occurred late in life and they may actually reflect the same phenomenon.

Berg: That is true. We find the same type of distribution curve for the onset of lesions as for mortality—in both rat and man. This is because the period for the full development of the disease, from the time of the early lesion to the late lesion, does not change with age.

Gerking: The correspondence between the shape of these curves, over a wide range of ages, is very remarkable.

Grüneberg: I have some confirmatory evidence on what you said about the relation between the age of onset of the disease and the environment. In mice of the A strain, in animals above a certain age, nearly all individuals suffer from the deposition of a substance called amyloid in the kidneys and various other organs. A group of investigators in the National Institutes of Health, Bethesda, has succeeded in influencing this condition by a change of diet. If these animals are fed on a protein-poor diet the onset of the condition is delayed and the total incidence is greatly reduced. Still more in

keeping with your results is the fact that if, in addition to the reduction in proteins, the total intake of food is reduced, amyloidosis in this strain can be made to disappear almost completely. In the A strain of mice there are three different entities which tend to kill these animals: (1) high incidence of mammary tumours (but only in breeding females), (2) high incidence of lung tumours, and (3) the deposition of amyloid. So far as I know the appearance of the other two conditions cannot be easily retarded.

To what extent were your rats inbred in these experiments, Dr. Berg? Were they genetically homogeneous or were you dealing with a mixed colony?

Berg: They were not homogeneous but were closely related. We have two lines of rats that have been randomly inbred for 65 generations. These derive from a small group of Sprague-Dawley rats acquired in 1945. Obviously, if the rats were more homogeneous the curves would be steeper than those we have shown.

Grüneberg: That being so, additional information might be obtained by using highly inbred strains of mice, which have very different lifespans. Some strains die early because they have an early onset of mammary tumours, such as the C3H strain; and the I strain has a short lifespan because it develops lesions in the stomach. Other strains differ in lifespan for reasons which are not yet fully understood. In addition one can use homogeneous but not inbred material (first generation hybrids) and segregating material (F_2 generations) and so on. It should also be possible to subdivide the causes of mortality further by systematic changes in the environment, particularly change in diet, as you discussed, but also by differences in crowding, temperature, etc. If this were done it would probably turn out that there is no unique life expectation of the species; presumably each genotype and each type of environmental situation has its own expectation of life, and in man the survival curve is presumably a superimposition of a whole family of curves.

Mühlbock: Amyloidosis is one of the major diseases in mice. In different inbred strains there are differences in incidence of amyloidosis. In some strains there is a very high incidence at 18 months of age, whereas in other strains it is nil, or very low. Therefore one should investigate a number of different strains before generalizing and saying that for that species this is the age of onset of the disease.

Berg: You are quite right. Our results apply only to our particular Sprague-Dawley strain, maintained under our conditions.

Sacher: Amyloidosis has been under investigation in our laboratory by Dr. S. Lesher (1957. *J. nat. Cancer Inst.*, **19**, 1119). He finds a high incidence in the A strain and in F_1 hybrids with an A-strain

parent. Amyloidosis in mice is a disease with maximum incidence in middle age. Incidence falls to zero in later life. Thus it resembles some diseases in man, particularly some liver diseases. If a single X-ray dose is given to the young animal, this whole sequence is moved to the left on the time axis so that a given incidence of amyloidosis is seen at an earlier age, and about the same total incidence is seen.

Perks: I was also struck by the symmetry of the curves of distribution of onset of the different lesions in your rats, Dr. Berg. We should bear in mind that when you combine symmetrical curves of this kind and get a curve of onset of lesions of all kinds, you do not necessarily reproduce symmetry. Further, as the mean delay between onset and death is significantly different for the different lesions, the final death curve could well be highly skew as compared with the component symmetrical curves of onset.

The other point I was particularly interested in was the delay in onset for females. My mind always goes to the question of the usefulness of statistics, and in the life assurance world we are seriously concerned with the differential mortality between males and females, particularly in view of the growing volume of pension business. In this country there is a difference of about five years in effective age between males and females at the older ages. In some of the Scandinavian countries there is a considerably narrower difference and the mortality for males is much lower than in this country. We actuaries do not really know why male and female mortalities differ, nor do we know why the Scandinavian male mortality is much more favourable than in this country, although some of us have thought in terms of environmental factors. It does seem to me that there may be some clue in the figures given here today. If, in fact, there is delay in the onset of some of these degenerative diseases in females as compared with males, maybe the answer is essentially constitutional.

Jalavisto: In Finland the excess of male over female mortality is about the highest in the world, especially in the 50-year-old group. This seems to be because coronary death is so common in Finland. I have the impression from Finnish data that at that age or in that sex which has a greater disposition for a certain disease, it is very difficult to lower the mortality in that disease by improving external conditions. For example, in cholecystic diseases in which females have a higher mortality than males, the reduction which has taken place in recent years is greater in the male—although in most diseases the reduction is much greater in females.

Perks: When I mentioned the Scandinavian countries I was not thinking so much of Finland as of the Netherlands, Denmark,

Norway and Sweden—countries which have an exceptionally low mortality amongst the males.

While your rats were in captivity and being observed, Dr. Berg, were they allowed their normal reproductive functions?

Berg: No. The experimental animals were kept separate from the breeders and were never mated.

Verzár: The rat colony kept in our laboratory has a 50 per cent survival rate at 23·5 months, even under very varying conditions. (This is, of course, not counting early deaths, since each mother is allowed to feed only four or five young ones.) Spontaneous death appears more frequently after the tenth month of age. The ages of

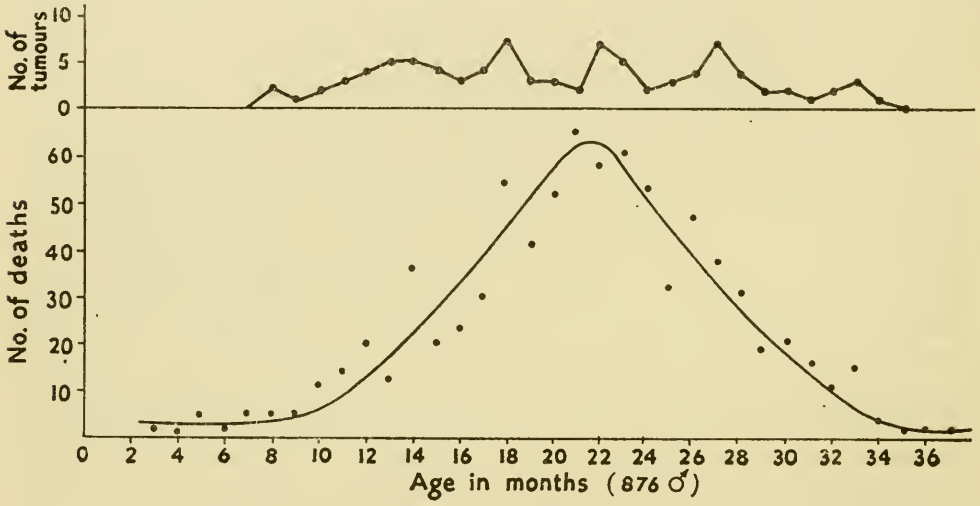


FIG. 1 (Verzár).

death of 1,602 rats (876 ♂ and 726 ♀) are shown in Figs. 1 and 2, which also show the number of tumours present in these animals. Tumours first appeared in 8-month-old animals, in both males and females. The number is much higher in females than in males but the occurrence is fairly constant during life. It decreases only between the 29th and 37th months, because so few animals survive. This means that the relative quantity of tumours in all deaths is smallest when the death rate is highest, i.e. between the 18th and 24th months.

The main cause of death was lung disease (bronchiectasis), in which the lung becomes infected and has large amounts of white pus. This is found in 24 per cent of females and 35·5 per cent of males. There are more tumours in females than in males (21 per cent against 11 per cent) and this difference thus counterbalances the greater

number of deaths due to lung disease in the male. Unexplained deaths were due to vertigo as signs of destruction of one labyrinth were found (9·5 per cent in females, 8·5 per cent in males). Other causes of death which were diagnosed account for about 16 per cent. We have no obvious cases of nephrosis leading to death, but all rats over the age of 10 months have proteinuria and this becomes very high in some very old animals. Very old animals, of about 36 months, generally show no pathological findings which could explain their death. The possibility exists, therefore, that natural death may

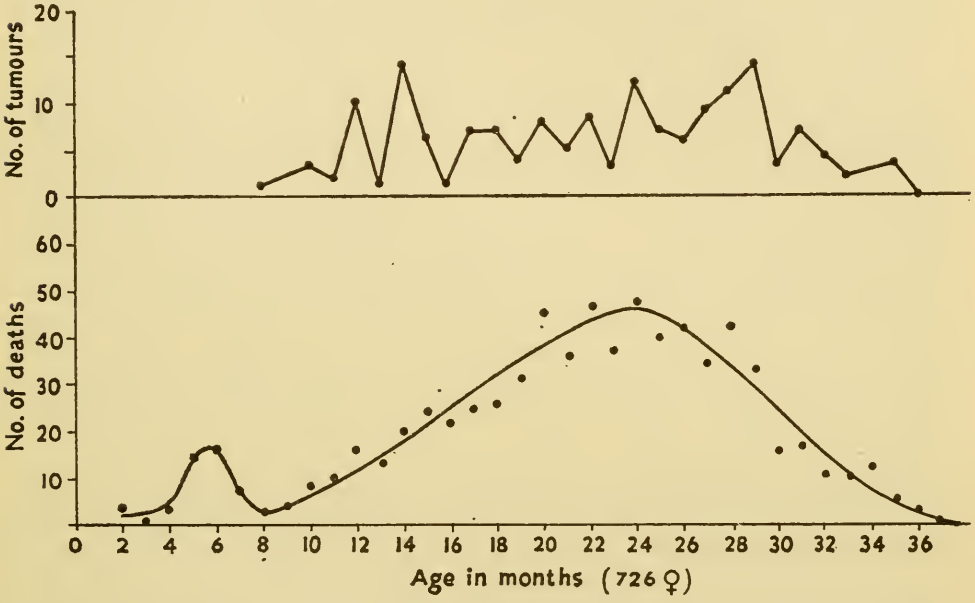


FIG. 2 (Verzár).

occur without obvious illness being suffered. (About 15 per cent of our rats were not autopsied.)

The survival curves show that after the 10th month "ageing" occurs at the same rate as resistance to external damage (infections) diminishes. This leads to maximal mortality at about 23·5 months, which is also the time of survival of 50 per cent of all individuals.

Another point is that creatinuria in our rats begins at 500 days, at exactly the same time as the muscular dystrophy in Dr. Berg's rats. Creatinuria is also present with old age in man.

Rockstein: How much, if at all, did you extend the life of those rats by restricted diets, Dr. Berg ?

Berg: Lifespan studies have not been completed. At 800 days the survival rate of *ad libitum*-fed males was 48 per cent as compared

with 87 per cent for restricted rats. Incomplete data indicate that the onset of lesions was delayed nine to twelve months.

Rockstein: What was the maximum weight attained ?

Berg: The body weight of restricted rats was 25 per cent lower than maximum weight of *ad libitum*-fed animals.

Rockstein: Is the protein content restricted to the same extent as the caloric value of this diet ?

Berg: The protein content of the diet was 20 per cent and was the same for the restricted diet.

Bourlière: Have you measured the basal metabolic rate in both restricted and unrestricted animals of the same age ?

Berg: No, I have not.

Comfort: In view of the interesting similarities between the lifespan curves in man and in rats, it pays to remember, when considering dietary restrictions, that there are differences in growth patterns between them. Your rats show virtually determinate growth, but under some conditions the rat grows in weight and in bone length for most of its life. This is a very different situation from that in man.

Berg: After 170 days, skeletal growth practically ceases in the rat though some of the epiphyses remain open for the entire lifespan. There is no evidence of osteogenesis in the cartilage plate of the tibial epiphysis of old rats. Increments in body weight of ageing rats are due largely to fat accumulation associated with prolonged inactivity.

Comfort: But my point was that in man you could not, I imagine, restrict growth. The effect of underfeeding on the growth pattern and on the appearance of sexual maturity in man may be different from the effects you can produce in rats. McCay kept his rats infantile for over 1,000 days; I doubt whether a comparable effect could be produced in man.

Berg: I think that if we had a comparable inbred strain of gluttonous men, and could perform a similar experiment, we might obtain results corresponding to those in the rat.

Tanner: I am accustomed to dealing with growth data rather than with data dealing with the other end of the lifespan. But methodologically there are very great similarities. We must consider, for example, the implications of the use of chronological age in all these data. One possible interpretation of your data could be as follows. We think of children or animals growing in the same way as we think of trains moving along a railway line. You can think of the various diseases as trapdoors on the railway line. You can either consider that those trapdoors have been moved nearer the start so that the train gets to them earlier, or you can consider that the

train has been slowed down and therefore does not reach the trap-doors, which have not altered their positions, until later. Your graph of the numbers dying, such as these that died before 800 days, somewhat supports the latter interpretation. You have got straight lines against age, but the slope of the line for the restricted rats is less than it is for the *ad libitum*-fed rats. This is the equivalent of the velocity of the train—to follow my analogy—being less. If you altered the time scale you could superimpose those two lines. This is a possible explanation, though not necessarily a correct one.

The specific question following that is how much was puberty, the opening of the vagina, actually delayed in your rats ?

Berg: There is a delay of about three to four weeks.

Tanner: That is relatively small. We do not really know how an animal measures the passage of time—except that it is not by a calendar ! We see this particularly in children, and we have various measures of what we call developmental age: the stage of ossification of the bones of the wrist, the number of teeth erupted, the menarche (the first menstrual period in girls) and so on. These stages are similar to the developmental horizons of the embryologists. It seems to me that in gerontology we are all badly in need of some equivalent of this.

Berg: We all recognize that various functions (such as sexual development, bone growth, and onset of lesions) take place more rapidly in lower animals than in man. This difference between species in rate of growth, development and ageing is a problem in itself. What we have attempted to do in our paper is to show the similarity between the species in that they follow the same laws in regard to onset of lesions and death.

Tanner: The growth curves of man and rodents (and your rodents, of course, are living in dreadful conditions) are really considerably different. But the growth curves of primates as a whole are very similar. This points out the tremendous importance of doing this sort of work with the cheapest monkeys you can get hold of.

Berg: The rats in our colony really live under very fine conditions. Except for being in captivity, they live under better conditions than most humans. However, the cost of these conditions is very high. A similar colony of monkeys would cost millions of dollars.

Comfort: Monkeys survive extremely poorly in captivity. Another trouble is the time factor. A baboon can live for over thirty years (Duetz, G. H. (1938). *Lab. Rep. zool. Soc., Philadelphia*, **66**, 31).

Verzár: You have just underlined one of the main points of gerontological research, Dr. Tanner—that we need tests of biological age. We speak far too little about tests, and all our work should

depend on them. You can all judge the age of a man, but how do you do it ? One form of tests in rats is adaptation methods: with ageing the power of adaptation, such as to cold, or lack of oxygen, decreases. You can also measure the age of the collagen in the rat's tail tendon (see Verzár, F. (1957). *Ciba Found. Coll. Ageing*, 3, 60. London: Churchill). But then it turns out that everything ages differently, and rats age differently in their brains than in their tendons. We irradiated rats with 700 r. and they died quickly, but their collagen had not aged.

Holt: I was going to raise the same point, because my experience is also in the comparison of growth curves which are completed at relatively different rates in different species. The dispersions of the age of incidence curves which you showed, Dr. Berg, in the comparison between man and rat, seemed proportional to their means. You thought that the curve for man had a higher dispersion because you were dealing in that case with a heterogeneous group; my interpretation was that both distributions were equally dispersed, because I mentally converted them to equivalent relative time scales.

Rotblat: Have you ever drawn graphs on which you plot age not in years but in the fraction of the span of life, so that you can compare the spans of life directly ? Otherwise how do you know that the onset of disease is the same in the rat as in man ?

Berg: Prof. Simms and I have discussed this extensively. He feels that such a plot would be meaningless. The lifespan is determined by the age of onset of lesions. Hence, to use lifespan as a standard for comparing age of onset would have no significance. It would be like comparing the speed of two racehorses—not in terms of minutes per mile—but in terms of minutes per mile multiplied by miles per minute.

Rotblat: From the change in the slope of the Gompertz curve which you showed us I would expect a large extension of the time scale.

Tanner: This works out as the equivalent in the human of around 17 to 18 years. In other words if you multiply the scale 30 : 1, which is roughly right, the curves you showed for the rat would be almost superimposable on those for man.

Rotblat: This is what I wanted to know: whether they are really the same if they are superimposed.

Maynard Smith: To me the most surprising thing you told us, Dr. Berg, was that the ages of onset for a whole variety of at first sight causally unrelated lesions were all shifted in the same direction by the same environmental treatment, i.e. restriction of the diet. I do not believe that one can tell very much about the causes of ageing in any

organism by just looking at curves. But if you experimentally interfere with the conditions and find that those curves move, then you do know something, and that seems to me very exciting. People working on mice have mentioned cases where specific diseases have been shifted to a younger or older age by specific environmental causes. What they have not discussed is whether either dietary restrictions or irradiation, or any other environmental treatment, have a common effect on a number of apparently unrelated diseases. If you delay one disease in the mouse by restricting diet, do you expect to delay the others or not ? This is of enormous theoretical importance and it may one day be of great practical importance.

Rotblat: It has been dealt with to a certain extent by Curtis, who has tried six different environmental effects (2nd International Conference on the Peaceful Uses of Atomic Energy, September 1958).

Sacher: Curtis reported only on the after-expectations, and not on the kinds of pathology present.

Maynard Smith: I want to know whether the ages of the onset of tumours, of kidney diseases, etc., are shifted in the same direction by the same environmental causes.

Berg: Yes. The delay in onset of all lesions including tumours produced by dietary restriction points to a single factor that controls the time of onset of disease.

Before the discovery of the tubercle bacillus the various forms of tuberculosis involving different organs were considered to be different diseases. With the discovery of the tubercle bacillus these conditions were found to be various consequences of a single cause. Although this analogy is not exact it is possible that a single mechanism may be involved in the onset of many widely different diseases.

Wigglesworth: An even better analogy is that of malaria. If you reduce malaria in a region the mortality from many other diseases is reduced.

Have you had the opportunity yet to switch over the diet at some stage of life in your experiments? In other words, is it indulgence in youth or indulgence in age which is significant in these effects ?

Berg: We are planning such experiments.

Comfort: I can think of two factors which could produce exactly such a non-specific effect on many diseases. One is the so-called stress response. I do not know whether you measured the adrenal weight in these creatures. The other is immunological; I am thinking of auto-immunization processes taking place in the body, and depending on the escape of cell antigens with the passage of time. Either of those could quite readily produce marked changes in many apparently unrelated diseases.

Berg: We do have adrenal weights but we have not studied them in relation to time of onset or incidence of lesions.

Comfort: Do these rats appear to produce more cortisone than the ordinary animal of that size ?

Berg: I do not look upon these restricted animals as being under stress.

Comfort: Even if you spend your life in a deck chair, dietary retardation is still a physiological stress. These animals have less to eat than they would normally have—although wild rats do not get all they want to eat.

Berg: Within certain limits a state of hunger in the restricted animal appears to be nearer normal for the rat than the satiety of the *ad libitum*-fed rat.

Comfort: It is still possibly a stress. The domestic rat is the result of selection for equanimity and low adrenal weight. Wild-caught rats are quite unmanageable. We have got laboratory animals which, whether we like it or not, have been adapted by covert selection to living under conditions of captivity.

Berg: We have in progress stress experiments based on variations in light, noise, and other unfavourable conditions. The adrenal weights of these rats will be compared with the adrenals of rats under standard conditions.

Tanner: Maynard Smith asked about the possible common mechanism whereby the times of incidence of these various diseases could all be brought forward together. I think that is rather a different situation from the amyloid disease one. As Comfort said, this somewhat nebulous concept of stress does provide a basis. I have recently been to the Mental Health Research Fund conference on "Stress in relation to mental health and disorder" at Oxford (1959. Blackwell's Scientific Publications, in press). Prof. Hans Selye was there and talked about stress as almost equivalent to ageing. The two concepts were being pushed very close together. Selye discussed some very interesting data on the effect of myocardial degeneration of various balances of deoxycorticosterone-type hormones and cortisol-type hormones. He evidently regarded the ordinary circulation of the blood as constituting a stress, while we would regard it as something which perhaps produces ageing. It is particularly in such endocrinological regulations that the general mechanism Maynard Smith is querying probably lies.

Sacher: Ionizing radiations, which are normally deleterious and shorten life, can in some circumstances increase life expectation, although without increasing the maximum lifespan. When this occurs in mice and rats, it is observed that the infectious diseases

that are enzootic in the particular populations (such as pneumonia in the rat, various kinds of enteric infections in the mouse) have a lower incidence in the irradiated populations than in the controls. What one sees then is a much more nearly rectangular life-table (less mortality in early and middle life) with no actual increase in the maximum span. L. D. Carlson, W. J. Scheyer and B. H. Jackson (1957. *Radiat. Res*, **7**, 190) at the University of Washington, Seattle, found evidence of this sort, as did E. Lorenz and co-workers (1954. *In* Biological Effects of External X and Gamma Radiation, ed. Zirkle, R. E, p. 24. New York: McGraw-Hill). They irradiated rats and mice, respectively, with small daily doses of gamma rays. We have obtained similar results at Argonne Laboratory (unpublished).

LIFESPANS OF MAMMALIAN AND BIRD POPULATIONS IN NATURE

F. Bourlière

Centre de Gérontologie Claude Bernard and Laboratoire de Physiologie, Faculté de Médecine, Paris

The various marking and banding techniques devised by mammalogists and ornithologists during the last 25 years have provided us with a good many data on the maximum lifespan of numerous species of mammals and birds belonging to a large number of families of these two classes of vertebrates. There are still too many gaps, especially for some groups peculiar to certain geographical areas (such as tropical species in general, small Australian marsupials), or for families with specialized ecology (as cetaceans among mammals and humming-birds or swifts among birds). Nevertheless we already have a preliminary idea of the potential lifespan of most families living in temperate countries.

When we turn from individuals to populations, the situation is far less satisfactory. Very few species of mammals and birds can indeed be aged accurately or have been marked in sufficient numbers and followed long enough to provide us with data which can be used to construct adequate life-tables of natural populations. There are none the less a few figures available and the purpose of this review is to bring together this scattered information, bearing in mind that most of the data at hand have been gathered haphazardly during ecological studies made for other purposes and that none of them are quite satisfactory from our present point of view.

The more accurate observations we have for mammals concern some of the larger ungulates which are of interest in game management in Western Europe and North America. All

these ungulates breed once a year, have a herbivorous diet and a long maximum lifespan. For such species sources of ecological data for the construction of life-tables are of three kinds: (1) knowledge of age at death for an adequate and reasonably random sample of the population; (2) knowledge

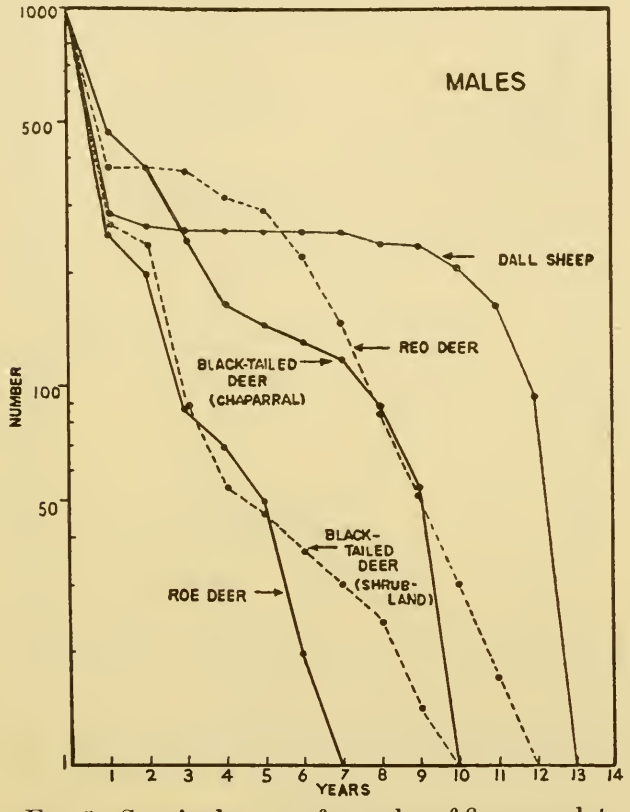


Fig. 1. Survival curves for males of five ungulate populations.

of the fate of individuals of a single cohort, at frequent intervals; and (3) knowledge of the age structure among the living. As Deevey (1947) pointed out, the first and third types of information can be used only if one is prepared to assume that the population is stable in time.

The survival curves of males and females of four species (roe deer, red deer, black-tailed deer and dall sheep), based on

the l_x columns in their life-tables, are shown in Figs. 1 and 2. Survival curves of both sexes taken together are given in Fig. 3 for barren-ground caribou. Original figures on which these calculations were based have been published by Evans (1891) for *Cervus elaphus* of the island of Jura off Scotland, by

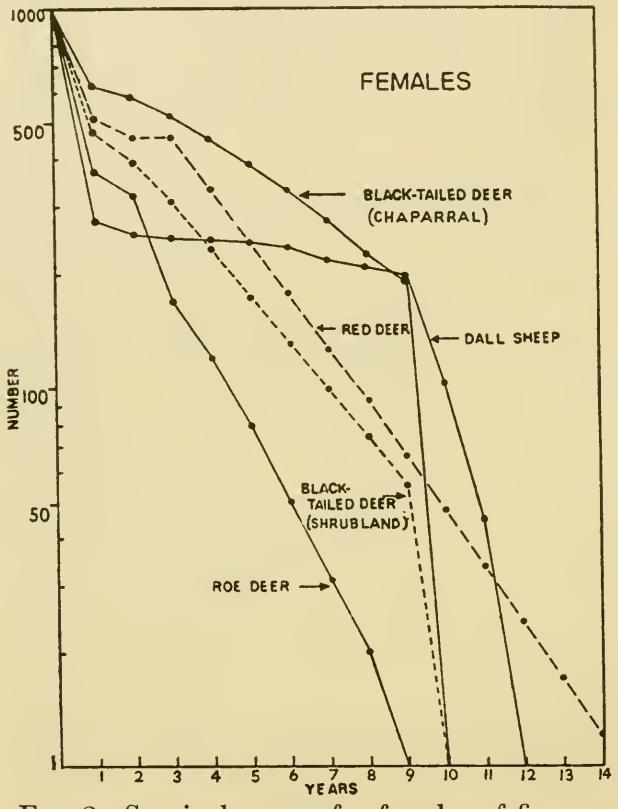


FIG. 2. Survival curves for females of five ungulate populations.

Murie (1944) for *Ovis dalli* of Mount McKinley National Park in Alaska, by Andersen (1953) for Danish *Capreolus capreolus* of the Game Research farm of Kalö and by Taber and Dasmann (1957) for *Odocoileus hemionus* of California. Data for Canadian *Rangifer arcticus* are from Banfield (1955). All these populations, except that of dall sheep, were hunted, either by sportsmen or natives.

When we compare these survival curves, we can quite clearly distinguish some interesting similarities and differences.

(1) A very steep initial slope, indicating a very high mortality during the first year of life, is found in both sexes of all the species. The actual mortality rate for calves is probably even greater, since their skulls are more easily overlooked and more

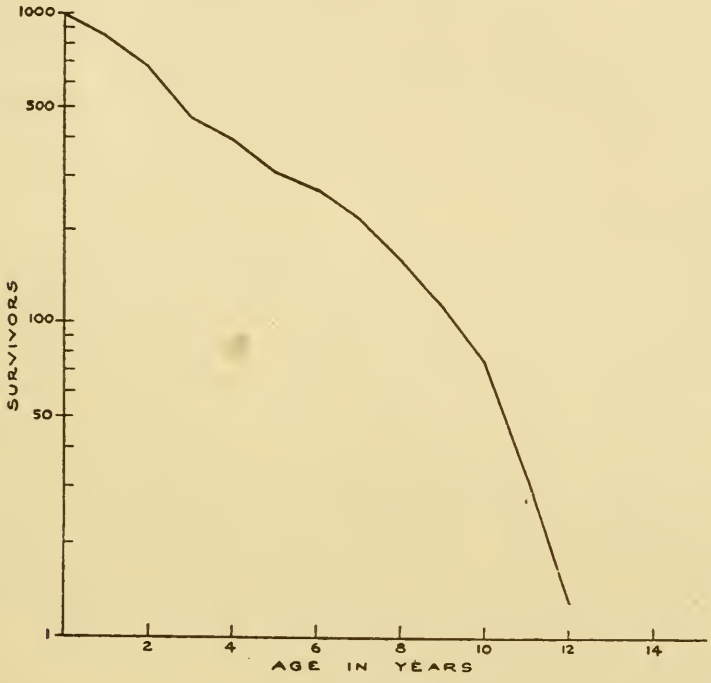


Fig. 3. Survival curve graduated on a logarithmic scale, for a series of 292 barren-ground caribou.

quickly destroyed than those of the adults. This age class is therefore quite probably under-represented in most samples.

(2) During the second year of life there is a small loss in both sexes of all species, with but two exceptions, that of the male roe deer where there is emigration and that of the male black-tailed deer of the Californian chaparral where some yearlings are killed.

(3) During the third year of life there is a heavy loss among male and female roe deer and male black-tailed deer from both

range types. The roe deer loss is due to emigration (Andersen, 1953) and that of the black-tailed deer to hunting (Taber and Dasmann, 1957). Among the male dall sheep and the male red deer there is little loss during the third year.

(4) From the fourth year onward, to old age, the hunted populations (roe deer, black-tailed deer and red deer) show fairly steep losses in both sexes. The rate of loss tends to lessen in full adulthood in the male black-tailed deer, presumably because learning and behaviour make these individuals less vulnerable to hunting (Taber and Dasmann, 1957). In the red deer, on the contrary, the rate of loss becomes heavier in full adulthood because of the selection of prime stags by sportsmen.

(5) The dall sheep, which is not hunted, shows very little loss from adulthood to 9 years old. If it were not for hunting, the other ungulate populations would probably exhibit survival curves rather more similar to those of *Ovis dalli*. As Taber and Dasmann (1957) pointed out, it is nevertheless doubtful that they could ever attain as high a survival as long as their ranges were fully stocked and starvation was a common cause of death. In that connexion, it is interesting to note that the survival curve of the barren-ground caribou, which is hunted mainly by natives, is closer to that of the dall sheep than to that of hunted deer.

(6) In old age there tends to be in most cases a steepening of the survival curve; this accelerated loss may be due directly or indirectly to senescence. In dall sheep we know, for instance, that both the very young and very old animals were preferably killed by wolves. Heavily hunted species do not display such a pattern because the high kill permits few individuals to grow old.

On the whole, it seems that most of the differences between these various populations of wild ungulates are not inherent in the species, but rather imposed by environmental conditions. If a roe deer population is fenced, emigration is prevented but winter mortality due to starvation becomes high.

In such a case, it would be expected that the population dynamics would be different from those found by Andersen (1953) in Kalö; the older animals would be competing with younger, physiologically more efficient animals. Similarly, if a dall sheep herd were not culled by predators, the population would presumably be limited by food supplies, and the mortality among prime adults would increase accordingly. Taber and Dasmann are thus certainly right in pointing out the danger of considering the population dynamics of a given animal under given circumstances as typical of that species in general.

All the species of long-lived and slow-breeding ungulates considered above, belonging either to hunted or unhunted populations, show in most cases age-specific mortality rates. The situation seems very different in small mammals, which are both short-lived and fast-breeding. All the species investigated so far appear to have age-constant mortality rates (after very early life).

In his study of the survival of wild brown rats on a Maryland farm, Davis (1948) shows, for instance, that no more than about 5 per cent of the rats live for a year. In the tropical environment of Malayan jungles, the situation looks very much the same for the 12 species or subspecies of Murids studied by Harrison (1956). Table I indicates the estimate of mean survival rates per month for marked animals, together with the mean and maximum length of life (in months) and the age at which only 5 per cent of the population can be expected to survive (effective maximum, 95 per cent).

The white-footed mice (*Peromyscus leucopus*) of the George Reserve in south-eastern Michigan have likewise a very low survival rate (Snyder, 1956). With the high rate of mortality of the winter 1950–1951, only one mouse in a thousand could be expected to reach an age of 93 weeks; with the lower rate of the previous winter, 34 mice could be expected to reach 93 weeks, and at least one would probably reach 197 weeks. The mean length of life from birth for such individuals would

be 17·4 and 31·5 weeks respectively. Such figures contrast sharply with a potential longevity of six to eight years, recorded in captivity.

The same situation occurs in the Tulare kangaroo rat. Fitch (1948) reported that 35·2 per cent of the *Dipodomys heermani* taken during a four-year live-trapping programme

Table I

SUMMARY OF SURVIVAL FIGURES FOR 12 SPECIES AND SUBSPECIES OF RATS IN MALAYA (AFTER HARRISON, 1956)

Species	*Survival rate per month*	*Length of life in months*		
		Mean	*Maximum recorded*	*Effective maximum 95%*
Chiropodomys gliroides	0·88	7·8		23
Rattus rattus diardii ♀	0·75	3·5		10·5
R. rattus diardii ♂	0·72	3·0		9
R. rattus jalorensis, sheltered	0·88	7·8	26	22
R. rattus jalorensis, scrub	0·76	3·6	14	11
R. rattus argentiventer	0·85	6·2	4	18
R. rattus jarak	0·90	9·0		28
R. exulans	0·73	3·2	9	10
R. mülleri	0·84	5·6	10+	18
R. bowersi	0·85	6·2		18
R. whiteheadi	0·75	3·5	9+	10
R. rajah	0·86	6·5	10+	20
R. sabanus	0·78	4·1		12
R. canus	0·82	5·0		15

had records that extended over not more than one month, 34·2 per cent had records of one to six months on the study area, and only 4·7 per cent had records extending for more than a year. The longest record was 33 months for an individual marked as a partly-grown juvenile. Other instances of short expectation of life at birth in wild rodents are reported by Blair (1953) and Bourlière (1954).

Larger rodents have a slightly longer mean longevity in natural conditions. Kalabouchov (1933) found that 31·5 per

cent of a population of little souslik (*Citellus pygmaeus*) reached the age of one year in the Caucasus and Fitch (1947) reported 9 to 38 per cent of cottontail rabbits reaching one year in central California.

Shrews appear even more short-lived than rodents. In England, Crowcroft (1956) estimated that the common shrew (*Sorex araneus*) lives for only 18 months at the longest and that most individuals die before reaching one year of age.

Bats, on the contrary, seem to have a higher survival rate than other mammals of similar size. The expectation of life in the colony of *Myotis mystacinus* ringed by Sluiter, Van Heerdt and Bezem (1956) in Holland, was 4·4 years, with a maximum lifespan exceeding 20 years! Such longevity is quite unexpected in such small mammals and probably has something to do with the very peculiar metabolic pattern of these animals.

To sum up the available data on mammals, it seems certain that, in natural conditions, small and fast-breeding species, with a low ratio of mean to potential duration of life, show very high and age-constant mortality rates. The only exception, that of bats, is probably due to the rather peculiar physiology of these animals. On the other hand, large and slow-breeding species, with a high ratio of mean to potential duration of life, tend to have age-specific mortality rates; this pattern is nevertheless strongly influenced by ecological conditions.

In birds, we find the same difference as in mammals between small and fast-breeding species on the one hand and relatively large and slow-breeding ones on the other. Most of the available data concerning this group have already been summarized by Lack (1954), Farner (1955) and Hickey (1955) and need not be mentioned again here. We will therefore limit ourselves to a few examples.

The best life-table we have for any bird of relatively large size is that of the common terns (*Sterna hirundo*) studied by

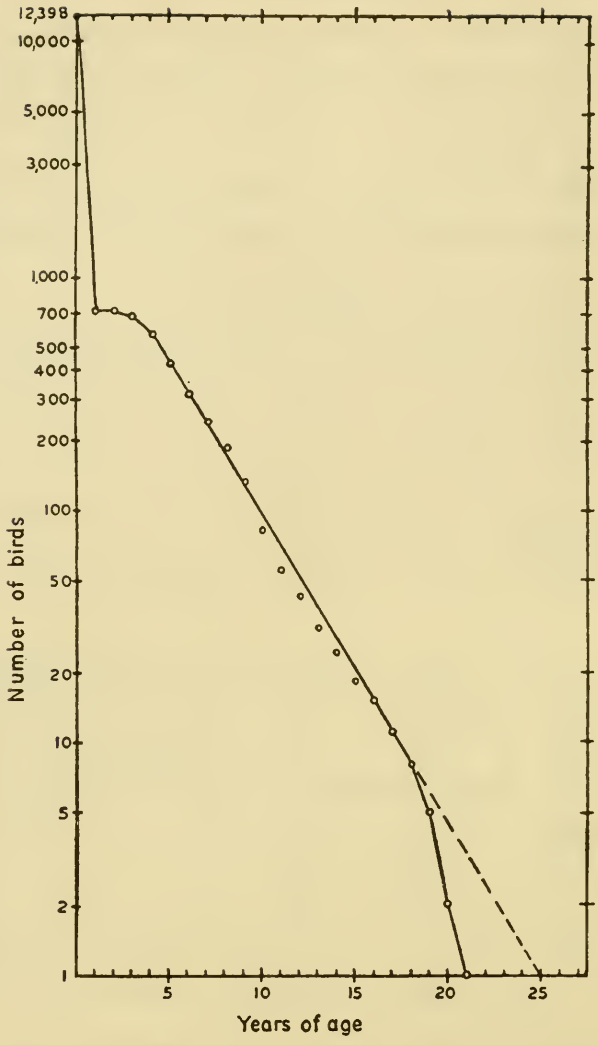


FIG. 4. Survival curve of a cohort of common terns banded as chicks in 1934 in Cape Cod colonies (After Austin and Austin, 1956).

Austin and Austin (1956). Adults (6,965) banded as chicks in the Cape Cod colonies were subsequently trapped in the same places by these ornithologists. To overcome the usual bias caused by band loss in long-lived sea birds, the Austins took the precaution of adding new bands to every bird wearing a band it had carried eight or more years. Their results are therefore more reliable than those of other observers. Fig. 4

shows the survival curve of a cohort of these terns which were banded as chicks in 1934.

In this sample, the first year mortality was over 94 per cent and the mean annual mortality rate from the fourth to the 18th year averaged 26 per cent. Beyond the 18th year the curve continues downwards, showing a steady increase in a mortality rate that had remained a straight line during the previous 14 years. The continuous rebanding of all the older birds handled during this study reduces the possibility that this sudden increase in the death rate can be explained by band loss; the Austins therefore consider that it might be due to senility. The composite life-table based on all the returns of common terns banded as chicks and trapped in nests by these observers, 1940 through 1955, shows the same increase in the death rate after the 18th year.

This tendency towards an increased mortality rate in old long-lived birds may be counteracted by a progressive improvement in the survival rate as the birds get older, at least in the species which are heavily hunted by man. Inexperienced immature or young adults appear to be shot much more frequently than older ones. Such an improvement in the survival rate of older individuals is quite apparent in the survival curve of Scandinavian buzzards (*Buteo buteo*), common herons (*Ardea cinerea*) and tawny owls (*Strix aluco*) drawn by Olsson (1958) and shown in Fig. 5.

In small and short-lived passerines, the situation is very similar to that of the small rodents and shrews, and the population turnover is very rapid. The mortality rate is always very high, especially at the nestling stage and in the first four months of life. Summers-Smith (1959) has found, for instance, a mortality rate of about 87 per cent for the juveniles (one to four months old) and about 40 per cent for the adults in the urban populations of house sparrows (*Passer domesticus*) he has studied. We have found even higher figures in a tropical population of the red-billed fire finch (*Lagonosticta senegala*) now under study in the lower Senegal valley. Kluijver (1951)

has found an average annual adult mortality of 49 per cent for great tits (*Parus major*) in Holland.

The lowest adult mortality rate for small birds is found among swifts, where it averages only 18 to 20 per cent per

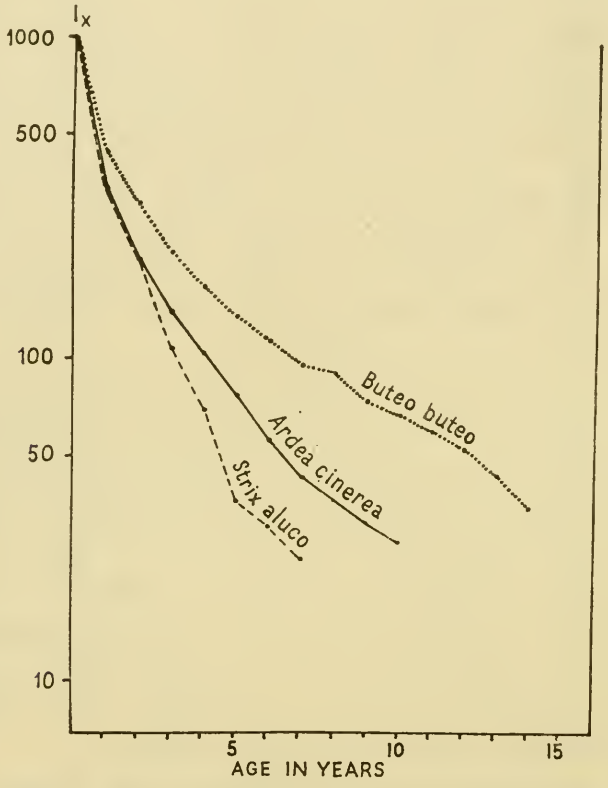


FIG. 5. The number (l_x) of surviving buzzards, herons and tawny owls at beginning of age group (x). Abscissa: Age in years. Ordinate: Numbers of surviving individuals, on a logarithmic scale.

year. It should be remembered that swifts, like bats, have a very poor temperature regulation.

The lowest figures in the whole class of birds are those of two sub-antarctic birds. In the yellow-eyed penguin (*Megadyptes antipodes*) population studied by Richdale (1957), the adult mortality rate was only 12·9 per cent per year; in the

royal albatross (*Diomedea epomophora*) this figure even goes down to 3 per cent. A summary of investigations on mortality rates in non-passerine birds is given in Table II (based on Farner, 1955 and completed after Bendell, 1955; Hickey,

Table II

Summary of investigations on mortality rates in non-passerine birds

Order	*Approximate range of juvenile mortality rates* %	*Approximate range of adult annual mortality rates* %
Sphenisciformes		13–30
Procellariiformes (Diomedeidae)		about 3
Pelecaniformes (Phalacrocoracidae)	35–80	12–30
Ciconiiformes (Ardeidae)	about 60	about 30
Anseriformes (Anatidae)	50–85	17–65
Falconiformes (Accipitridae)	about 60	about 30
Galliformes	20–50	50–83
Charadriiformes (Charadrii)		15–50
(Lari)	40–60	18–30
Columbiformes (Columbidae)	about 80	55–58
Strigiformes (Tytonidae)	50–79	28–57
(Strigidae)	about 50	about 30
Apodiformes (Apodidae)	about 30	18–20

1955; Lack, 1956; Richdale, 1957; Boyd, 1957, 1959; Summers-Smith, 1959; and Southern, 1959). The adult mortality rates given there apply after the first 0·5 to 1·5 years, according to the species or groups concerned. The juvenile mortality rates are calculated for a year beginning with the fledgling leaving the colony, or sometime later during the summer of hatching.

We therefore find very much the same dichotomy in birds as in mammals, between small and fast-breeding species on the one hand and large and slow-reproducing ones on the other. The highest ratio of mean to potential lifespan is indeed found in a bird, the royal albatross, which reproduces only every second year and may reach an age of at least 25 years in the wild.

Reproductive and mortality rates are thus closely adjusted. Both vary mainly with ecological conditions and an increase in mortality rate in older individuals, which may be due to the onset of old age, is apparent only in large, slow-reproducing and long-lived birds and mammals.

REFERENCES

ANDERSEN, J. (1953). *Dan. Rev. Game Biol.*, **2**, 127.
AUSTIN, O. L., and AUSTIN, O. L., Jr. (1956). *Bird Banding*, **27**, 55.
BANFIELD, A. W. F. (1955). *Canad. J. Zool.*, **33**, 143.
BENDELL, J. F. (1955). *Canad. J. Zool.*, **33**, 195.
BLAIR, W. F. (1953). *Advanc. Genet.*, **5**, 1.
BOURLIÈRE, F. (1954). The Natural History of Mammals. New York: Knopf.
BOYD, H. (1957). *Bird Study*, **4**, 80.
BOYD, H. (1959). *Ibis*, **101**, in press.
CROWCROFT, P. (1956). *Proc. zool. Soc. Lond.*, **127**, 285.
DAVIS, D. E. (1948). *Ecology*, **29**, 437.
DEEVEY, E. S. (1947). *Quart. Rev. Biol.*, **22**, 283.
EVANS, H. (1891). Some Account of Jura Deer. Derby, privately printed.
FARNER, D. S. (1955). *In* Recent Studies in Avian Biology, p. 397. Urbana: University of Illinois Press.
FITCH, H. S. (1947). *Calif. Fish Game*, **33**, 159.
FITCH, H. S. (1948). *J. Mammal.*, **29**, 5.
HARRISON, J. L. (1956). *Bull. Raffles Mus.*, **27**, 5.
HICKEY, J. J. (1955). *In* Recent Studies in Avian Biology, p. 326. Urbana: University of Illinois Press.
KALABOUCHOV, N. I. (1933). *Rec. Trav. Sci. Univ. Moscou*, **1**, 29.
KLUIJVER, H. N. (1951). *Ardea*, **39**, 1.
LACK, D. (1954). The Natural Regulation of Animal Numbers. Oxford: Clarendon Press.
LACK, D. (1956). Swifts in a Tower. London: Methuen.
MURIE, A. (1944). The Wolves of Mount McKinley. Washington: U.S. Dept. Int. Nat. Parks Service.

OLSSON, V. (1958). *Acta Vertebratica*, **1**, 86.
RICHDALE, L. E. (1957). A Population Study of Penguins. Oxford: Clarendon Press.
SLUITER, J. W., VAN HEERDT, P. F., and BEZEM, J. J. (1956). *Arch. néerl. Zool.*, **12**, 63.
SNYDER, D. P. (1956). *Misc. Publ., Mus. Zool. Univ. Mich.*, **95**, 1.
SOUTHERN, H. N. (1959). *Ibis*, **101**, in press.
SUMMERS-SMITH, D. (1959). *Ibis*, **101**, in press.
TABER, R. D., and DASMANN, R. F. (1957). *Ecology*, **38**, 233.

DISCUSSION

Rotblat: Is anything known about the lifespans of the same species in captivity ?

Bourlière: Not for the swift, because it is at present impossible to keep them caged. What we have are good figures on the maximum lifespan of some individuals. We also know that in both large and small mammals and birds the maximum lifespan in captivity is always far greater than in the wild. Nevertheless, in wild populations, at least in those species for which we have data, a very small percentage of very old individuals is found; but in order to find these very scarce old animals, you need to study a very large population for a very long time.

Rotblat: I understand that bats kept in zoos live much longer than the 20 years which you mentioned for the albatrosses.

Bourlière: Twenty-five years is the longest recorded lifespan for the royal albatross in the wild in New Zealand, but as far as I know, nobody has ever kept an albatross in captivity for more than a few years because it is very difficult to feed them.

Comfort: A chaffinch has been kept for 29 years (Moltoni, E. (1947). *Riv. ital. Orn.*, **17**, 139), and even an inbred budgerigar is reported to have reached nearly 20.

Scheidegger: One swift in a big colony near Basle lived for 18 years, but the rest had an average age of about 5 to 6 years.

Danielli: Your remarks about birds which survive longest being large does not fit in with data for the swift, as you pointed out, Prof. Bourlière. Do you attribute the advantage the swift seems to possess to the fact that it more or less hibernates ?

Bourlière: That explanation was advanced by Farner (1955) and it may be true because we have the very same phenomenon in mammals. We may compare rodents and bats of similar size and weight. Small mice, for instance, never live in captivity or in the wild for more than four years, whereas bats of the same weight will live for 20 years; so there is certainly some correlation between a long

maximum lifespan and the ability to lower the body temperature and the basal metabolic rate for more or less prolonged periods.

Danielli: Have experiments been done in which groups of animals which normally hibernate have been prevented from doing so ?

Bourlière: At the present time I know of no good observations which have been made on mammals. The difficulty is not only to house a large number of animals during 30 or 40 years, but also to secure an investigator who could study such a problem for three decades.

Danielli: Even if one did, of course, you would still be up against some difficulty in interpreting the facts, because it seems to me that the advantage which is gained may either be that the "biological time-scale" is altered by hibernating, or alternatively the hibernating animal may be protected from all accidents and so forth. One does not know which of these two alternatives is involved.

Comfort: Many small birds presumably die in winter. If a species hibernates it has not got to search for food, and so it is not so liable to die from lack of it.

Bourlière: In swifts there is no true hibernation during winter, because they migrate to tropical Africa at that time of the year, but their temperature control is nevertheless very different from that of passerines. The studies on swifts which have been made in Oxford and Switzerland by D. Lack and E. Weitnauer have shown (see Lack, 1956) that during bad weather, especially in early spring when the parent swifts are unable to obtain enough flying insects to feed their young, the young then undergo a kind of pseudo-hibernation or torpid stage instead of dying as other species do. J. Huxley, C. S. Webb and A. T. Best (1939. *Nature* (*Lond.*), **143**, 683) have described the same feature in adult humming-birds at night, and they are also long-lived animals. One humming-bird lived in captivity in the Copenhagen Zoo for more than eight years, which is quite a record for a bird so difficult to keep in captivity.

Danielli: Humming-birds might be the right material, as they have this diurnal "hibernation".

Maynard Smith: In the terns there was a very low mortality in the second and third years of life. Is this associated with the fact that this species does not breed until its fourth year ?

Bourlière: Yes, common terns do not return to breed in quantity until their fourth summer.

Sacher: Have the life-tables of animal populations in wild-life preserves, such as the European and American bison, been studied ?

Bourlière: As far as I know, no such studies have ever been made on bison in America or in Europe. The first good study on the

behaviour and ecology of the American bison was published a year ago (McHugh, T. (1958). *Zoologica, N.Y.*, **43**, 1), and we are still waiting for a similar work on the European form. The so-called wild European bison are in fact so domesticated that they are not a good example to study. If you want to have samples large enough to be studied, you need to choose rather common species which can live in national parks or some place where human disturbance is very rare. That is why most of the available information has been drawn from the field of game management or rodent control.

Chitty: Did you say there was no age-specific mortality rate for small rodents in the wild ?

Bourlière: I do not know of any study showing such an age-specific mortality rate in wild rodents.

Chitty: I do not really see how this kind of information could be obtained very easily for wild populations. Such evidence as I have published (1952. *Phil. Trans. B.*, **236**, 505) shows that there is a higher mortality rate with increasing age but of course it is exceedingly difficult to separate the environmental components from it. There is an increase in mortality rate as the winter goes along, but it is not known whether that is because of changing ecological conditions, or because of an increase in average age.

Kershaw: This may be compared with observations on insects in the wild. There seems to be evidence now that the survival of insects with a rapid population turnover is modified by predators and natural hazards, whereas those with a long and slow population turnover maintain their own intrinsic survival. In mosquitoes it seems likely that the intrinsic survival, having a Gompertz function with a sloping straight line, is altered completely by field conditions, and has a flat Gompertz function. For the last ten years we have been studying the life-cycle of one of the West African flies, *Chrysops*, which turns over once a year. In the laboratory that fly has a normal rectangular survival, both in those bred from the pupae and in wild-caught flies. We have been following through natural populations of flies coming in to bite man, which of course is a selective, but functionally selective, population. We have found that throughout the year the population is made up of separated successive cohorts, each behaving with its own particular rectangular survival, so that in this particular fly the intrinsic survival is the natural one. I think one has to go back to mosquitoes now that one has biological markers for them, based on parity and so forth, to see whether what is true of *Chrysops* is also true of mosquitoes. This, of course, is of importance in producing mathematical models.

ARTERIOSCLEROSIS IN BIRDS

S. Scheidegger
Institute of Pathology, University of Basle

Arteriosclerosis ranks first among diseases affecting the arteries, and it is of much more importance in human beings than in animals. All experiments designed to produce such a form of degeneration in the vessels of animals are doubtful, since a severe form of this disease can only be found in man. In animals we never find such severe forms as regards the spreading of the disease or transformation of the tissue, and it can never be described as a disease producing clinical symptoms. In other words, whereas arteriosclerosis is one of the principal diseases in man and a frequent cause of death, in animals it is only of secondary significance, showing only slight malformations, possibly with transformation of the vessel wall. The term arteriosclerosis, which etymologically means a hardening of the vessels, in fact stands for a combination of different lesions. At the onset of the disease, we only find some inclusions in the wall. In the final stage there is accumulation of degenerations, malformations, and transformations; all layers of the vessel walls are now affected and we can see calcifications, ossifications, and often an occlusion of the lumen. In other cases the same calcification and ossification process can produce an enlargement of the vessel. At the beginning of the illness we can see a series of various reactions of unknown and doubtful origin. Some forms of arteriosclerosis constitute pure inflammations, whereas some can be classified as pure degenerations. In some cases this disease of the vessels is restricted to a single organ or to a specific system, i.e. it may be found only in the vessels of the heart, or the vessels of the brain, or perhaps the finer vessels

of the extremities. It is a known fact that the vessel can be affected in various ways. The disease can be a diffuse one, and then the whole vessel is in an arteriosclerotic state. Alternatively, the severe degeneration of the vessel—often the arteria coronaria—is restricted to small defined areas. With this form, we speak of a so-called arteriosclerosis in plaques. Furthermore, we know—and this is another important factor—that the organ has an influence on the development and type of arteriosclerosis. In the brain, for example, we never find the same forms of vessel degenerations as in the kidneys or in the heart. In the brain vessels, especially in the finer vessels of the brain substance, we never find atherosclerosis with deposits of fat and cholesterol esters, etc. In this organ we have a more diffuse hyaline transformation, in others fine fibrillar changes, a so-called fibrillar vessel degeneration, similar to that which can be seen in the neuroglial tissue (of the neurofibrillar changes and in the senile plaques of the Alzheimer disease). This form, which Scholz (1938; Scholz and Nieto, 1938) was the first to describe, is a typical malformation of the brain vessel. The final stage is always the same: the occlusion of the vessel. This occlusion is the only pathological symptom which can be found. The pathological process and the way of evolution can, however, vary.

In most observations of arteriosclerosis it is not possible to give a key to its origin and development. We know that arteriosclerosis of the vessels of the heart, which develops only in restricted areas, is often the result of an inflammation whereas the diffuse forms mostly result from a primary pure degeneration. Experimental studies of this disease are not possible. It is possible that some types of arteriosclerosis are the cause of either an acute or a chronic arteritis. The acute arteritis can in turn be the result of an infection with bacteria or with toxins. In the place of the inflammation of the vessel wall, parietal thrombi develop. The bacterial infections may disappear. After the inflammation a degenerative form of arteriosclerosis may occur. An injured vessel wall, or

infiltration by parasites, can often be the causative factor in chronic arteritis. Domestic animals, especially cattle, dogs and pigs, show a slight thickening of the arterial walls through proliferations of the intimal tissue. Scherer (1944) describes a case of a 20-year-old chimpanzee with sclerosis of the main vessel of the brain without degeneration of the tissue. In four *Macacus rhesus* monkeys the same author could observe fine degenerations of the cortex of the brain with multiple small areas showing a softening of the tissue. In the cerebellum the granular layer was in a state of degeneration with multiple areas in which the cells had disappeared. In birds more severe forms of such degenerations can be seen. Two different phenomena may be the cause: some species of birds reach an advanced age, and some are (and this is another important fact) purely carnivorous. The distribution and the anatomy of arteriosclerosis in birds present some difficulties. In most cases the aorta is the seat of the malformation. The aorta valves are free of lesions. In the intima layers we often find hyperplasia with an increasing of fibres. The media shows a muscular granularity in this part of the vessel wall. Microscopical examination of such vessels shows a media with ruptured muscle fibres and and a split or broken elastica. The intima is often covered with a fibrocellular exudate.

One of the best and most complete reports on the problem of arteriosclerosis in birds has been published by Fox (1923), who gives a survey of the different types of diseases affecting the animal in captivity and in the wild state. To illustrate the problem the author has collected some thousands of post-mortem examinations in the Washington Zoo. Psittaci have a high percentage of arterial disease. Some findings are of interest. Often the central vessels are not the principal seat of an atheromatosis as in other classes, and the lesion shows reactions with tissue proliferation. Accipitres have the greatest percentage of any order. The arterial lesions are frequently accompanied by renal, myocardial, and valvular disease. Degenerations are equally severe in the media and intima.

Calcifications are not seldom found in this group of birds. In parrots the arterial damage is caused in the arteria carotis or in the small wing arteries, but the most common seat of the process is the lower thoracic region. Galli often demonstrate a vascular disease combined with myocardial disease. Cormorants, pelicans and gannets often have arteriosclerotic malformations and intimal proliferations. Ducks and geese present a considerable number of cases which demonstrate arteriosclerotic degenerations accompanied by cardiac and general pathology. The character of the lesions is similar to that found in the Accipitres. Arteriosclerosis is common to many zoological orders. Fox gives a good general review of this problem. The order of percentage incidence is Accipitres 6·6; Anseres 3·4; Psittaci 1·8; Galli 1·6; Passeres 0·22. Carnivorous birds have the highest incidence of chronic arterial disease. Next in order are the ungulates, the anserine birds and the carnivorous mammals. Fox remarks on the interesting fact that the orders with great activity, such as the primates and the passeres, are at the end of the list. This is perhaps due to the fact that their food consists chiefly of carbohydrates.

Arteriosclerosis in mammals and birds in captivity is often accompanied by nephritis, chronic infectious disease or chronic enteritis.

In some cases of this disease, aneurysm in the vessels can occur. This develops above the valves and arises from a degenerative arteritis. The present author has examined cases of birds with slight, medium, and severe arteriosclerosis. These observations are all autopsies in the Basle Zoo. The animals were vultures, storks, cranes, flamingoes and geese.

Milder forms of this disease are quite common. In these cases the aorta showed a thickening of the intima and plaques could be seen, especially where the main vessels branch off. In these parts we found small deposits of fat or a pure fibrosis without cholesterol deposits or atheromatous ulcerations. (See Figs. 1–10.)

In all the cases observed the elastic membranes were split off or interrupted. In the medium forms of atherosclerosis yellow areas could be seen in the vessel wall and with increasing age the disease became more severe.

Wolkoff (1925) described a typical arteriosclerosis in a 40-year-old parrot. Observations of arteriosclerosis in a 35- and a 42-year-old parrot with severe atheromatosis are reported by Nieberle (1931), Nieberle and Cohrs (1931), by Pallaske (1930), and by Beneke (1931). In his thesis Fahr (1935) discussed arteriosclerosis in chickens.

The comprehensive article written by Krause (1939) about the pathology of animals states that the beginning of the aorta is not the place of the primary degeneration. He found that in most cases the principal seat of this disease was the part of the aorta between the kidneys. He reported that in his observations atheromatous ulcerations could never be seen. The intima was always intact, hardened and thickened by a fibrosis. Inflammatory processes are not of importance. In his opinion lipoidosis and sclerosis are two different processes. He found the primary infiltration of fat in the aorta between the kidneys, never in the aorta ascendens or in the arcus aortae. Such forms of degeneration could be observed in 5 to 6-year-old poultry. A calcification could very seldom be found. He suggests that only in some cases with avitaminosis or hypervitaminosis can a primary necrosis produce small calcareous deposits.

Fahr (1935) suggests that no connexion exists between the degree of the infiltration of fat and age. Sclerosis is, however, a process that can only be found in advanced age. He was never able to see a coronary sclerosis. In these studies of arteriosclerosis in birds only one animal developed an arteriosclerotic disease of sufficient clinical significance to cause severe functional disturbances. A vulture nearly 60 years old developed an arteriosclerotic disease with such clinical symptoms as can be found in man. The cause of death was a diffuse vascular sclerosis. All the different stages could be

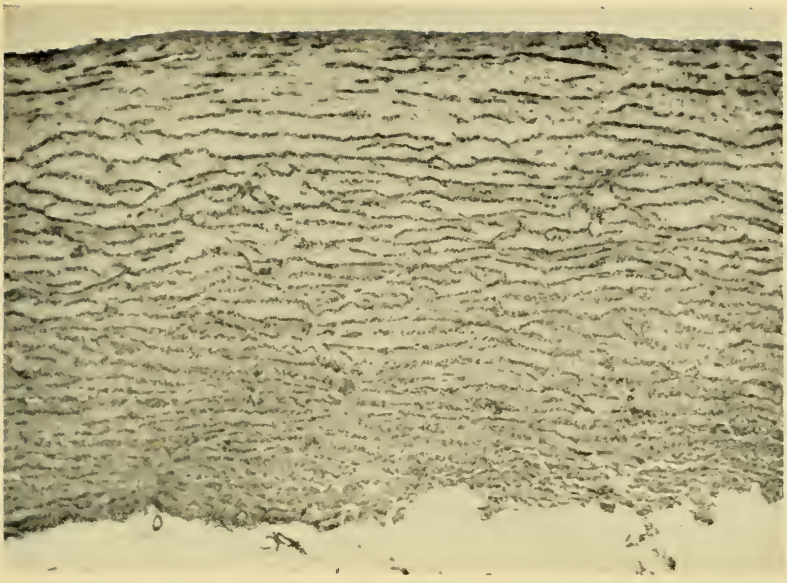


FIG. 1. Diffuse pure mucoid degeneration with a fine lipoidosis in the arteria carotis (*Sarcorhamphus gryphus* L.).

FIG. 2. Diffuse thickening of the aorta by infiltration of mucoid and fat substances with degeneration of the elastic membranes (*Balaeniceps rex* Gould).

facing page 110

FIG. 3. Arteriosclerosis of the basilar artery. Thickening of the intima with degeneration of the media (*Sarcorhamphus gryphus* L.).

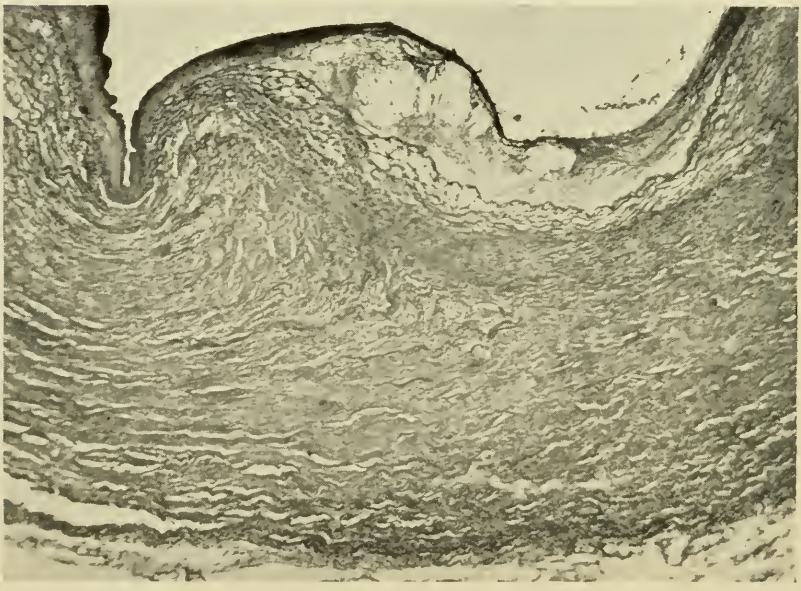


FIG. 4. Coronary vessels with a fine thickening of the intima and deposits of cholesterol esters and fat (*Sarcorhamphus gryphus* L.).

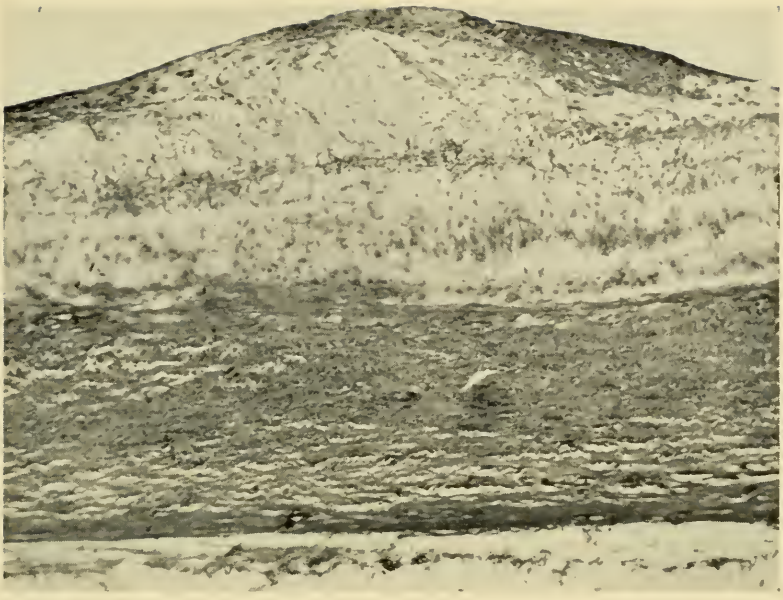


FIG. 5. Diffuse infiltration of mucoid substances in all the different layers of the vessel wall, with degeneration of the media (*Phoenicopterus*).

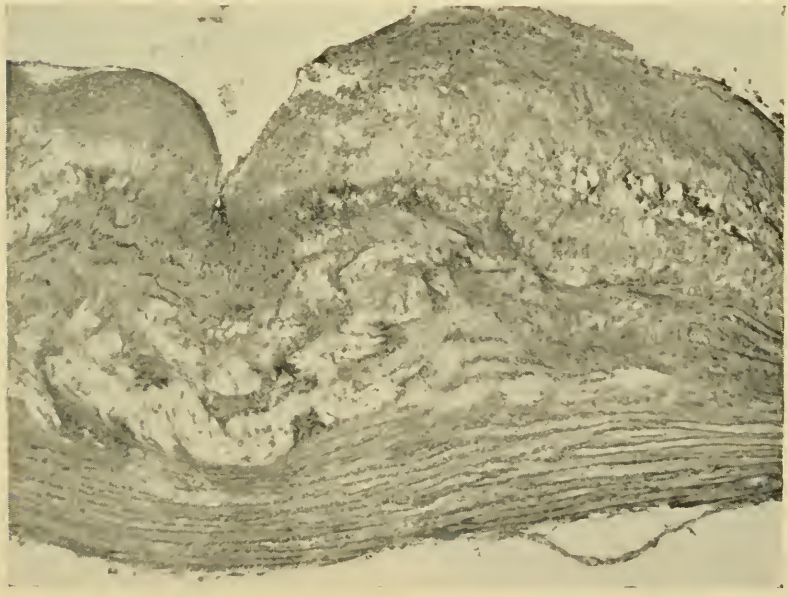


FIG. 6. Aorta of the red-breasted goose with degeneration of all the different layers of the vessel wall and a splitting off of the elastic membranes in the media (*Branta ruficollis* Pall.).

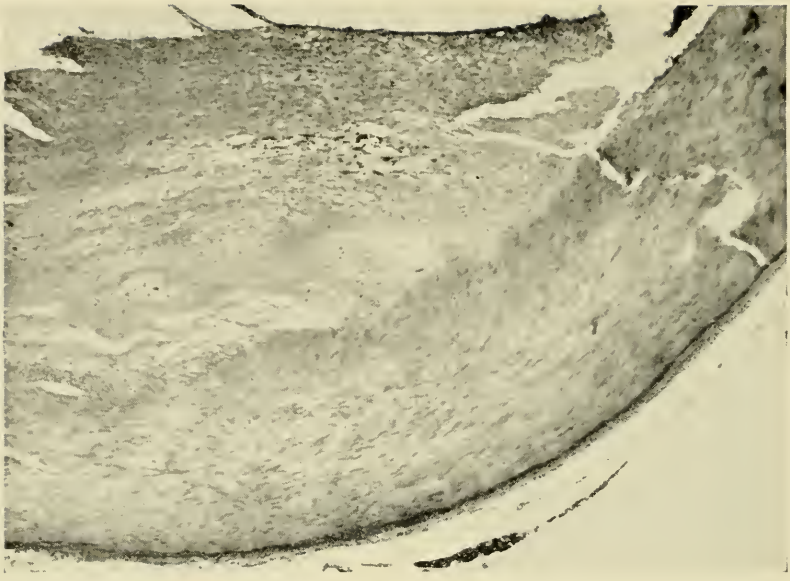


FIG. 7. Thickening of the media and intima with a fine calcification and multiple small deposits of cholesterol esters (*Balaeniceps rex* Gould).

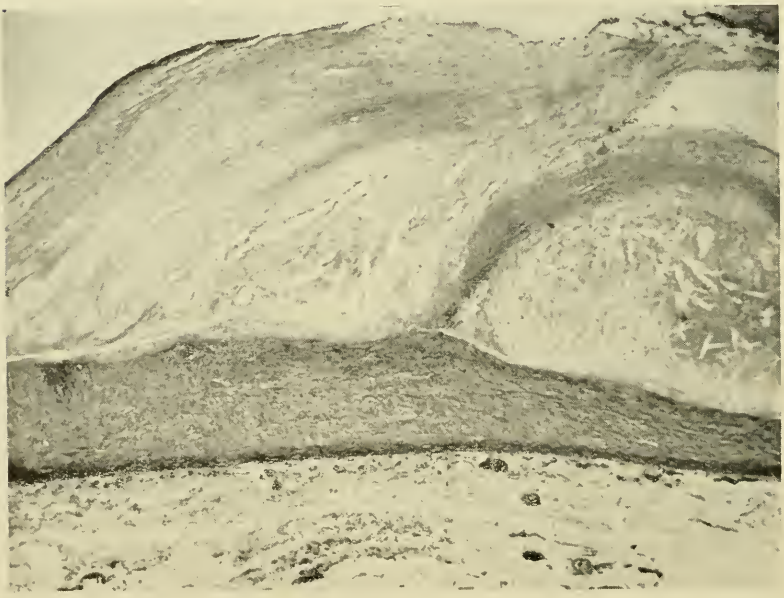


FIG. 8. Severe thickening of the arterial wall by large deposits of fat and cholesterol esters (*Balaeniceps rex* Gould).

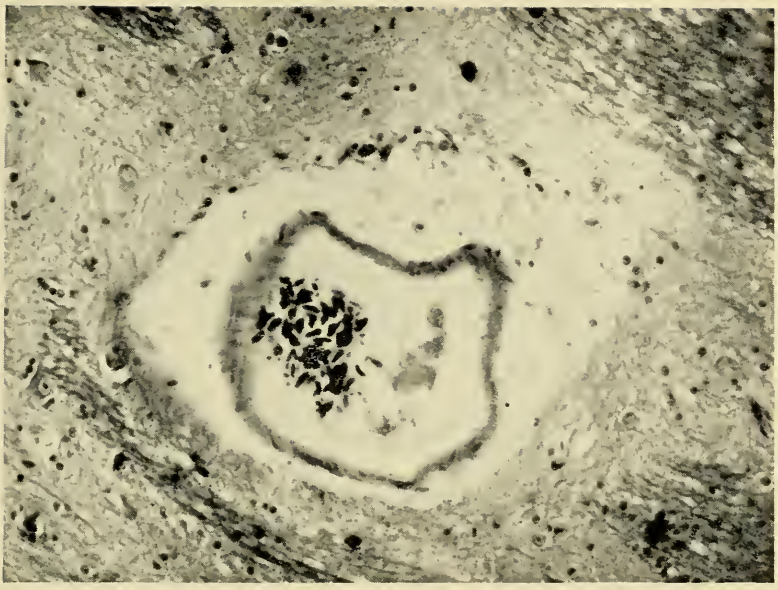


FIG. 9. Vascular hyalinosis with perivascular softening (*Sarcorhamphus gryphus* L.).

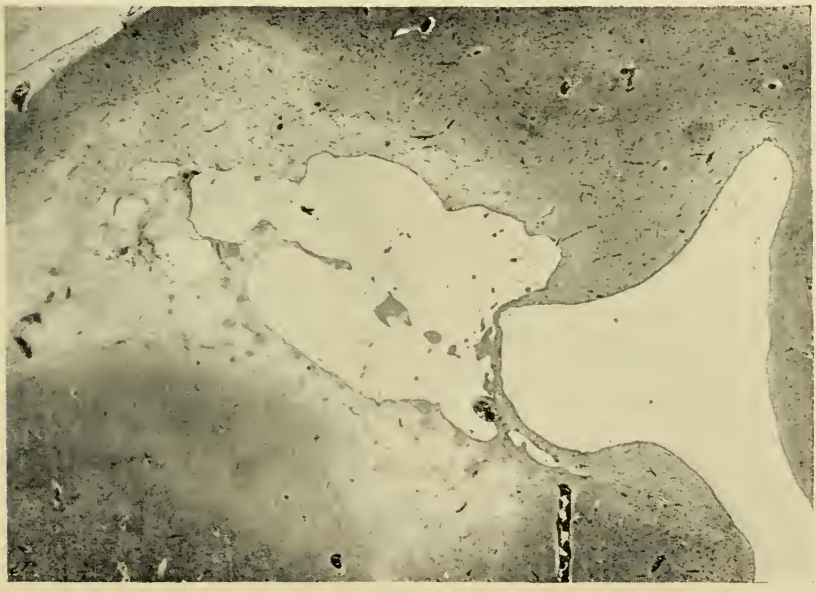


FIG. 10. Sections through the brain of a vulture showing post-malacic cyst secondary to cerebral arteriosclerosis, with enlargement of the lateral ventricle (*Sarcorhamphus gryphus* L.)

seen in this case: proliferations of the intimal cells, with concentric lamellations which completely filled the lumen, hyaline transformation, swelling and necrosis of the media, compression of the lumen, medial calcification and ossification. Atheromatous plaques were found in the main vessels. In the observation under review the concentric lamellations and the necrosis of the media produced a compression of the lumen of the vessel which was accompanied by a softening of the brain with subsequent formation of cysts. The coronary vessels showed a high degree of arteriosclerosis. The lumen was often nearly obstructed by intima proliferations. Several infarctions of the myocardium could be seen.

The present author's suggestion is that only in captivity can such severe forms of arteriosclerosis occur. In nature the animal concerned would have died earlier of hunger since the higher functions of life would have been handicapped. The atherosclerosis induced by several conditions in animals may be reversed by removing those conditions but there is no evidence that the same possibility exists as far as the disease in human beings is concerned. Atheromatosis in the human adult must be considered as irreversible. Atherosclerosis is induced in rabbits and chickens by adding cholesterol in large quantities to the food. But animals species differ greatly. The concentration of cholesterol in the blood is a very important factor in atherosclerosis both in the human being and in animal species. Atherosclerosis can be seen in any artery but the major concern is the coronary artery. It is common in young persons, and quite common in persons over 30, but this type of degeneration cannot be seen, or extremely rarely, in animals.

Arteriosclerosis is of much more importance in human beings than in animals. This fact is important. Unfortunately there is no possibility of studying this disease which so frequently affects the human being, in animal experiments.

REFERENCES

BENEKE, R. (1931). *Beitr. path. Anat.*, **87**, 285.
FAHR, H. O. (1935). Dissertation: Giessen.
FOX, H. (1923). Disease in Captive Wild Mammals and Birds. Philadelphia: Lippincott.
KRAUSE, C. (1939). *Ergebn. allg. Path. path. Anat.*, **34**, 226, 367.
NIEBERLE, K. (1931). *Verh. dtsch. path. Ges.*, **26**, 239.
NIEBERLE, K., and COHRS, P. (1931). Lehrbuch der spez. path. Anatomie der Haustiere. Jena: Fischer.
PALLASKE, G. (1930). *Frankfurt. Z. Path.*, **40**, 64.
SCHERER, H. J. (1944). Vergleichende Pathologie des Nervensystem der Säugetiere. Liepzig: Georg Thieme.
SCHOLZ, W. (1938). *Z. ges. Neurol. Psychiat.*, **162**, 694.
SCHOLZ, W., and NIETO, D. (1938). *Z. ges. Neurol. Psychiat.*, **162**, 675.
WOLKOFF, K. (1925). *Virchows Arch. path. Anat.*, **256**, 751.

DISCUSSION

Verzár: Was there any difference in the diet of the birds which had arteriosclerosis and those which had not ? Diet is important in view of the present theories that arteriosclerosis is connected with fatty acids.

Scheidegger: All these birds are carnivores, and it seems to me that this is one of the most important factors in arteriosclerotic disease. The birds all came from the Basle Zoo, and this form of arteriosclerotic disease is seen especially in vultures, flamingoes, cranes and so on. I have never seen severe forms of arteriosclerosis in other birds than the kinds mentioned here.

Bourlière: Can it really be said that arteriosclerosis in birds is always related to a carnivorous diet ? European flamingoes are "mud-eaters", feeding mainly on small crustaceans and invertebrates, and these kinds of food should contain a lot of unsaturated fatty acids. Geese also feed as much on plants as on invertebrates. In some zoos flamingoes may receive a different diet than they do in the wild.

Scheidegger: In Basle Zoo the flamingoes ate crustaceans and so on, and they also received small pieces of meat in this food. I do not know about geese.

Hinton: I know there are a lot of differences between arthropods and the rest of the animal kingdom, but small crustaceans are bits of meat, aren't they ?

Rockstein: Arteriosclerosis has been observed in the common fowl, of course, and it is primarily a herbivore, so I do not think one can generalize so easily on this point.

Lindop: There are two studies going on in this country on atherosclerosis in poultry (Saxl, H., in press; Hall, D. A., in press). One is done by the Ovaltine workers who are keeping two groups of animals on identical diets, but one group has limited exercise. These groups are being followed for the development of atherosclerosis. The other study, at Leeds, is more on the cytological and the biochemical side. There they have been able to produce atherosclerosis in poultry which have limited exercise, and they have also been able to reverse atherosclerosis in poultry which have been allowed to exercise after they had been inhibited. Atherosclerosis developing in zoo animals might therefore be caused by the comparatively limited exercise they get.

Scheidegger: The problem really concerns the age of these birds. This old vulture lived in the zoo for about 56 years. It came as a young bird, at the age of 3 or 4 years, and the food was always the same. In its last year the bird had severe arteriosclerosis. The ages of the other birds are not known, and I cannot tell you what the birds had to eat in captivity.

Jalavisto: Orma has made observations on cholesterol-fed poultry and it seems that even a little exercise may be enough to retard development of atherosclerosis. He put the food on one side of a fence, and the water on the other side. The poultry drink after they have eaten and therefore have to go over the fence and back again all the time. That could be very easily arranged in a zoo, and it would be one means of checking easily whether it is exercise or something else which is operative in this case.

Nigrelli: Arteriosclerosis and atherosclerosis can be induced experimentally by dietary methods in poultry, as Dr. Lindop said, and I think there is some relationship with the pantothenic acid in the diet.

Comfort: The blood pressure of these birds in relation to their configuration may have some effect. It is just conceivable that birds of the flamingo type, which have both a long neck and a considerable change of posture between their head-erect and head-down positions, have larger fluctuations in blood pressure than other animals. It is a point which needs investigation.

The other point is that I am quite sure all zoo birds and animals are better fed, or more consistently fed, than they are in the wild. I rather suspect that, like Dr. Berg's rats, these birds would be less likely to get atherosclerosis if they were only fed intermittently. I suspect that in the wild the vulture does not feed every day, or even every week, unless he is lucky.

Bourlière: I understand that a study is already under way in

South Africa concerning the blood pressure of the giraffe. It was found to be extremely high, but as far as I know no increase in arteriosclerosis was observed in that species, at least in the wild.

Comfort: There is the slight drawback that the giraffe is such an extremely timid animal that even in a zoo it is a nightmare to file its hooves, or anything like that—you have to give it an anaesthetic. It must be rather a difficult animal on which to estimate the blood pressure, unless you could telemeter it.

Rockstein: The birds which show this atherosclerotic condition seem to be among the longest-lived birds. For example I have here records of a common crane which lived to more than 42 years, a flamingo to more than 22, a stork to 30, and a vulture to close to 60 years of age. The question is whether atherosclerosis is indeed a factor in longevity as such ?

Berg: Prof. Scheidegger's presentation underlines again the necessity of knowing causes of death in lifespan studies. Important, too, is the question of whether degenerative diseases are inevitable with ageing.

Kershaw: The Royal Air Force has been doing routine post-mortems on its fittest people—those who fly jet planes. Most of these are aged around 19, 20, and 21. In the coronary arteries of these men a high and astonishing degree of coronary atheroma was found. Whether that means that most of us have vessels which have atheroma in them which is of no significance, or whether that particular selected group is more likely to have atheroma, is not clear.

Danielli: It should be perfectly easy, shouldn't it, to get post-mortems on the average young adult killed in an accident ?

Kershaw: The difficulty lies in getting comparable objective reports.

RELATION OF LIFESPAN TO BRAIN WEIGHT AND BODY WEIGHT IN MAMMALS*

GEORGE A. SACHER

Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Illinois

MY interest in the comparative study of lifespans stemmed from the realization that the zoological literature contains a wealth of data that can be used to analyse the factors governing ageing and longevity in mammalian species. In this paper I shall first describe a statistical analysis of the relations of lifespan to brain and body weight, and then enter into a discussion of the theoretical issues. These considerations have been alluded to briefly in previous communications (Sacher, 1957, 1958).

The objective of the empirical analysis is to establish the quantitative dependence of the lifespans of mammalian species on the body weights, brain weights, and metabolic rates of adult representatives of these species. This is in effect a study of allometric relationships, in which lifespan is regarded as a physical dimension of a species on the same footing as the linear or mass dimensions. In this paper the species lifespan is defined as the maximum documented longevity for that species. With a few exceptions the lifespan data come from domesticated animals or from zoo animals.

There were two reasons for using the lifespan rather than the life expectation. The first is that satisfactory estimates of the life expectations even now are available for only a few domesticated species and for an even smaller number of

* This work was performed under the auspices of the U.S. Atomic Energy Commission.

captive species (Comfort, 1956, 1958). Second, when data come from animals kept under very different environmental conditions the lifespan is a more stable longevity parameter than is life expectation. This is clearly seen in the life-tables

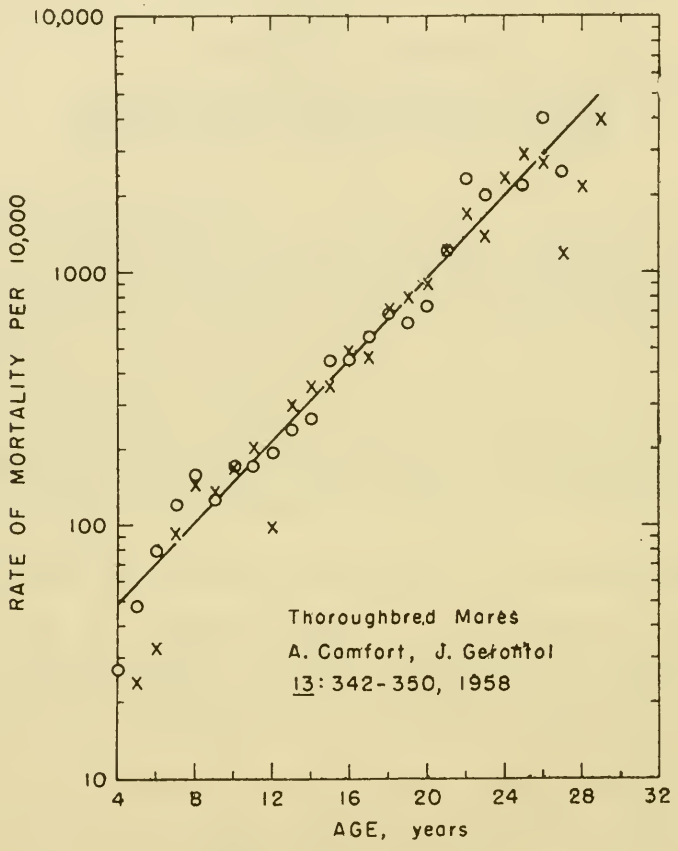


FIG. 1*a*. Logarithm of age-specific rate of mortality plotted versus age (Gompertz plot). Data on thoroughbred mares from Comfort (1958). A life-table for which the Gompertz plot has a straight-line relation to age conforms to the Gompertz equation $q_x = Ae^{\alpha x}$.

of human populations in different countries or in the same country in different historical periods. Instances can be found in which life expectations vary by more than a factor of two, but even in these extreme cases the lifespans do not differ by

as much as 20 per cent. There is a good reason for this, as will be discussed below.

One objection that has been raised to the use of lifespans is that the estimated lifespan will increase as the sample on which the estimate is based increases. Until recently there was no comprehensive statistical treatment of this question. With the publication of Gumbel's (1958) treatise on the Statistics of Extremes, we now have a statistical theory that is adequate to deal with most questions that arise. The *characteristic oldest age* (the age attained when one survivor remains of the initial cohort) is an easily computed statistic in terms of which we can discuss the dependence of lifespan on cohort size. If the survivorship curve is of the Gompertz type, in which the age-specific rate of mortality increases exponentially with age, the characteristic oldest age increases as a double logarithmic function of the cohort size. This is illustrated in Fig. 1, where the characteristic oldest age is shown in relation to cohort size for an actual life-table of the Gompertz type, drawn from Comfort's analysis (1958) of the life-table of thoroughbred mares. It can be seen that increasing the cohort size by a factor of 10^5 would increase the characteristic oldest age by only one-third. The lifespan itself, i.e. the age *at death* of the oldest survivor, would vary more slowly than this.

The typical mammalian life-table can be adequately described by the Gompertz–Makeham equation, in which the relation of rate of mortality to age contains a constant term in addition to the Gompertz term:

$$q_x = Ae^{\alpha x} + B \qquad (1)$$

The Makeham term, B, is markedly influenced by environmental conditions, whereas the Gompertz term is influenced to only a small degree. However, the Gompertz term will always dominate at advanced ages, and the lifespan therefore tends to behave like an extremum statistic of a Gompertz life-table. Since the inherent ageing parameters characteristic of the species are embodied in the parameters A and α of the

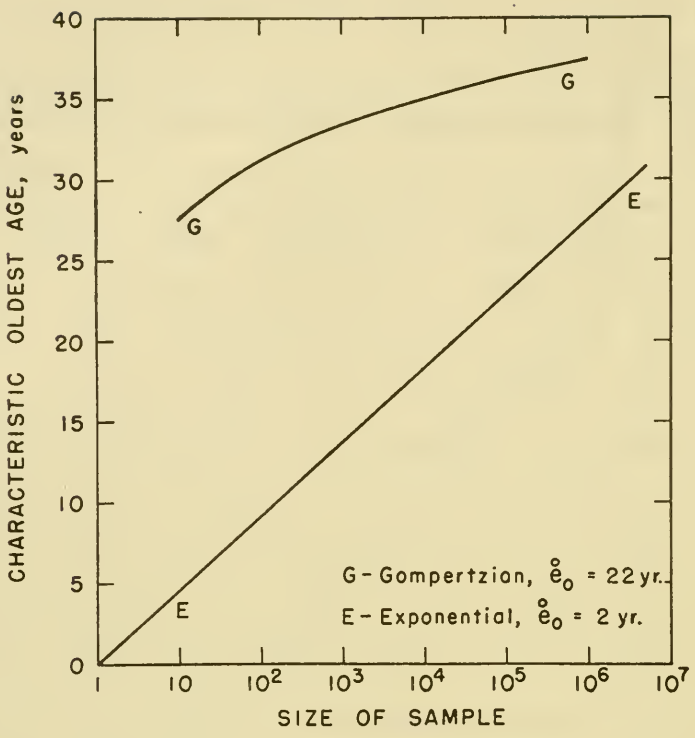


FIG. 1*b*. Relation of *characteristic oldest age* to size of initial cohort. The curves drawn are for a Gompertzian life-table (see text) and for an exponential life-table. The curve for the Gompertzian populations is representative of the amount of variation of lifespan with sample size that might be expected in populations of domestic or zoo animals kept under good conditions. The line for the exponential population is illustrative of the relation of lifespan to sample size that would hold for populations under very heavy environmental pressure, such as small birds or rodents in the wild.

Gompertz term* it follows that the lifespan is the preferred statistic for the characterization of species longevity.

* It can be argued that the life expectation should be preferred precisely because it measures the response to environmental as well as intrinsic factors. There can be valid reasons for preferring the life expectation in certain contexts, and especially in the discussion of evolutionary or ecological adaptations. However, the present paper is addressed to the question of intrinsic limitations on length of life, and these questions are appropriately discussed in terms of measures that are as nearly as possible invariants for the species, independent of environmental influence.

The theory of extremes can be used to compensate for the bias introduced by very great differences in cohort size. This has not been attempted in the present study.

The data on brain weight and body weight were taken from the extensive compilations of these values by Count (1947),

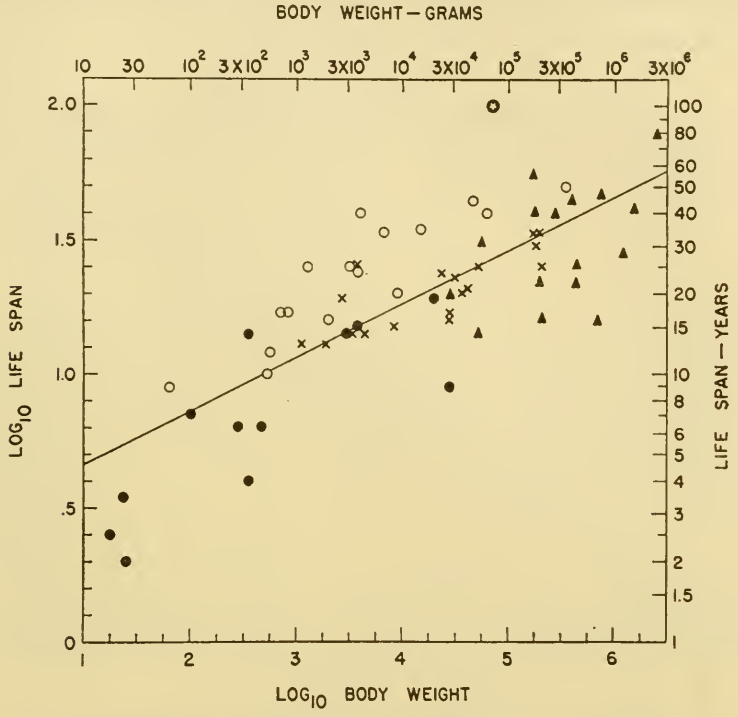


Fig. 2. Relation of lifespan to body weight for 63 species of mammals. Data plotted on double logarithmic grid. The symbols denote groups of species as follows: open circles—primates and lemurs; solid circles—rodents and insectivores; crosses—carnivores; solid triangles—ungulates and elephants; star in circular field—man.

von Bonin (1937), and Quiring (1950). The body weights and brain weights are in some instances averages of values reported by two or more investigators. Lifespans are the maximum records encountered in the sources examined, and were obtained principally from the compilations by Bourlière (1946), Comfort (1956), Flower (1931), Walker (1954), and Yerkes and Yerkes (1929).

There are 63 species for which body weight, brain weight and lifespan values were tabulated. Most orders of placental mammals are represented, the most important omissions being the bats and marine mammals. Common logarithms of the numbers were used in the statistical analysis. Simple and multiple linear regressions were computed. The statistical

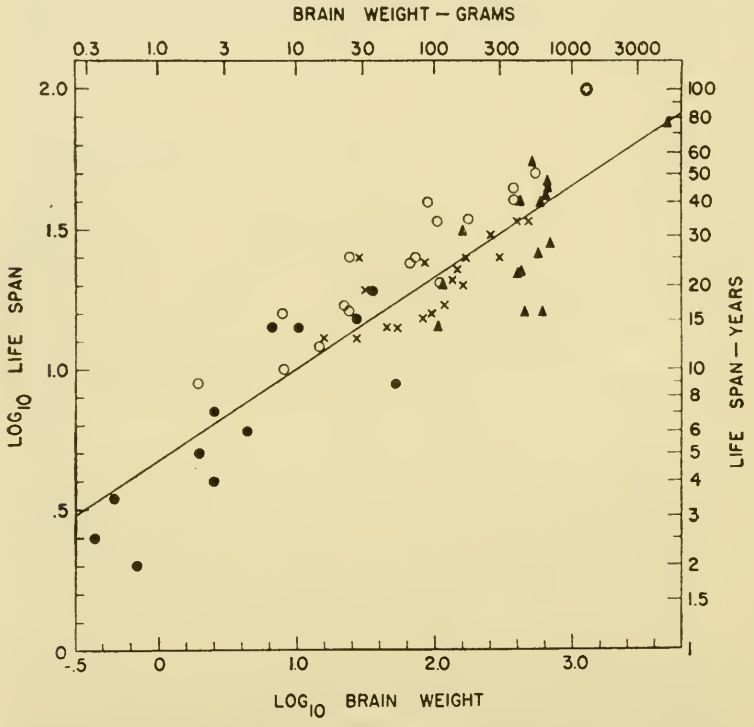


FIG. 3. Relation of lifespan to brain weight for the same 63 species shown in Fig. 2. Symbols as defined in legend to Fig. 2.

formulae are presented in lucid fashion by Hald (1952). Appendix 1 contains the means and standard errors of the variables, the regression coefficients and their standard errors, the total variances of the variables, and their residual variances after removing the variance in regression. With the information provided the total, partial and multiple correlation coefficients can also be computed.

The relation of lifespan to body weight is exhibited in Fig. 2, with the points plotted on a log-log grid. The species are divided into four groups, each comprising one or more orders, and each group has a distinguishing symbol. No use is made of this subdivision in the statistical analysis since the data were not sufficient to justify a separate analysis by orders; such analysis will be undertaken when more extensive data are collected.

It can be seen that there is a highly significant relation between lifespan and body weight. The relation of log lifespan in years (x) to log body weight in grams (y) is found by least squares to be (see also Appendix 1b)

$$x = 0{\cdot}198y + 0{\cdot}471 \qquad (2)$$

This regression accounts for 60 per cent of the variance of lifespans. It can also be seen that the different groups are stratified in the diagram, with the rodent lifespans lying below the regression line, those for carnivores and ungulates more or less evenly distributed around the line, and those for primates lying almost entirely above.

A similar diagram showing the relation of lifespan to brain weight is displayed in Fig. 3. The least squares regression of log lifespan (x) on log brain weight in grams (z) (Appendix 1c)

$$x = 0{\cdot}325z + 0{\cdot}684 \qquad (3)$$

accounts for 79 per cent of the lifespan variance. This is significantly greater than the variance reduction brought about by regression on body weight, so it can be concluded that brain weight by itself is a better predictor of lifespan than is body weight. The superiority of brain weight over body weight as a predictor is manifested by a reduced scatter between the groups (shown by their clustering closer to the regression line) and also by a decreased scatter within groups (shown by the smaller dispersion of the individual deviations from the mean deviation for the group). There is still evidence of stratification, however, so that brain weight does not by itself account for all the extractable lifespan variance.

Next we may ask whether lifespan can be predicted more accurately by a combination of brain and body weight than by either of them alone. The answer to this question is given by the multiple regression of lifespan on body weight and brain weight (Appendix 1d),

$$x = 0{\cdot}636z - 0{\cdot}225y + 1{\cdot}035 \qquad (4)$$

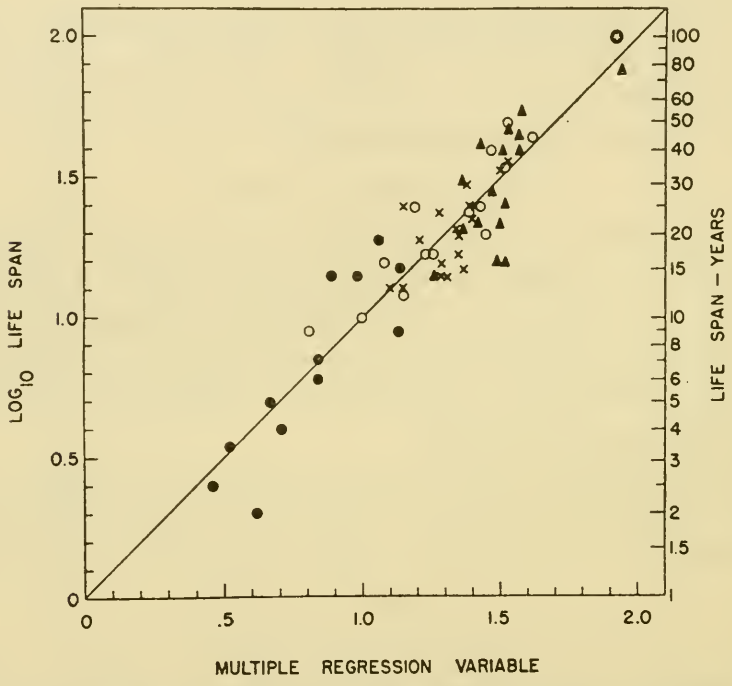


FIG. 4. Relation of lifespan to multiple regression variable defined by Equation (4) or Equation (8). Symbols as defined in legend to Fig. 2.

This regression removes 84·4 per cent of the lifespan variance. This is not a significant increase over the 79 per cent removed by regression on brain weight alone. However, the scatter diagram (Fig. 4) suggests that the multiple regression has further reduced the differences between groups. It is possible that a more detailed statistical analysis, in which a separate allometric relation is obtained for each of the major taxonomic

subdivisions of mammals, will further increase the goodness of prediction, since Figs. 2, 3 and 4 give evidence that the relation of brain weight to body weight for the different groups cannot be described by a single allometric relation. Count (1947) is only the last of a number of authors to point this out.

Discussion of the independent rôles of brain and body weights will be facilitated by the use of a transformed variable. Brain weight and body weight are closely related variables, for the regression of brain weight on body weight (Appendix 1e)

$$z = 0{\cdot}666y - 0{\cdot}888 \tag{5}$$

accounts for 91·7 per cent of the brain weight variance. The deviation of an individual brain weight value from the regression line is the logarithm of that fraction of the brain weight of the species that is independent of the overall regression of brain weight on body weight. This deviation is defined to be a new variable, w, which is given by the equation

$$w = z - 0{\cdot}666y + 0{\cdot}888 \tag{6}$$

This quantity is called the *index of cephalization*. It should be understood that this is by definition a measure of brain development that is orthogonal to body weight. The definition contains none of the *a priori* considerations that have frequently entered into the definition of this quantity since the time of Dubois (1924). Von Bonin (1937) has urged that the index of cephalization be defined in this objective fashion.

The regression of lifespan on index of cephalization (w) is found to be (Appendix 1f)

$$x = 0{\cdot}636w + 1{\cdot}283 \tag{7}$$

By the definition of w, the regression coefficient for x on w is numerically equal to the partial regression of x on z in Equation (3). However, the variance of w is but 8·3 per cent of the variance of z. In consequence the sampling error of b_{xw} is larger than that for $b_{xz.y}$ (Appendix 1f), and the variance removed by the regression of x on w is 23 per cent rather than

84 per cent (Appendix 1). However, the coefficient of regression of x on w is more than four times larger than its standard error, so the regression is highly significant.

The multiple regression of lifespan on body weight and index of cephalization is found to be (Appendix 1g)

$$x = 0{\cdot}636w + 0{\cdot}198y + 0{\cdot}471 \qquad (8)$$

It will be noted that the partial regression of x on y in Equation (8) is numerically equal to the coefficient of total regression of x on y in Equation (2). This follows from the fact that y and w are orthogonal variables, so that the regression of x on y is completely independent of, and unaffected by, the regression of x on w.

One further dimension of mammalian constitution that has been measured for a large number of species is that of metabolic rate. The great amount of data accumulated by many investigators, and especially by Rubner, Benedict and Brody, has been masterfully organized in Brody's treatise on Bioenergetics and Growth (1945). Brody has shown that the relation between basal or resting metabolic rate and body weight for warm-blooded vertebrates (including birds) follows a power law relation with great precision. The regression of logarithm of specific metabolic rate, m (in calories per gram per day), on log body weight is (Appendix 1h)

$$m = -0{\cdot}266y + 1{\cdot}047 \qquad (9)$$

The correlation coefficient is over 0·99 (Brody, 1945). In view of this high correlation, the partial regression of specific metabolic rate on index of cephalization must necessarily be small. We can therefore assume tentatively that this correlation is zero and substitute m (given by Equation (9)) for y in Equation (8). The resulting equation for the regression of lifespan on metabolic rate and index of cephalization is

$$x = 0{\cdot}636w - 0{\cdot}744m + 1{\cdot}252 \qquad (10)$$

Sampling errors and residual variance for this relation cannot be given.

It can be concluded that two independent factors are required to account for the observations. One of these may be identified by the highly correlated pair of variables—metabolic rate and body weight. The other factor may be identified by the index of cephalization, which is orthogonal to body weight and must also be nearly orthogonal to metabolic rate (see above). Both of these factors are represented in the brain weight, so that brain weight alone is almost as good a predictor of lifespan as brain weight and body weight combined.

Although the existence of two independent factors is very reliably established, their resolution into the two orthogonal terms specified above is not unique. The extension of these procedures of multivariate analysis to larger sets of anatomical and physiological variables may make it possible in future to identify these factors more confidently, and perhaps also to establish the existence of one or more additional factors governing length of life.

In spite of the coarseness of the measures used, this first statistical investigation of the allometry of lifespan has been rewarding. Much more remains to be learned from a more detailed examination of these relations within individual orders of mammals, and also in other vertebrate classes, birds in particular. It is to be expected that the numerical values of the coefficients will differ in these different groups, for brain function can be specified by a single number such as total mass only to the degree that brain structure is describable in all its anatomical details by a single allometric coefficient. These same considerations apply to the somatic dimensions.

This completes the discussion of the statistical analysis and the implications of these findings for the theory of ageing in mammals will now be considered.

First, let us consider the above findings in terms of a theory of ageing put forth by Rubner almost exactly a half-century ago (1908). He took note of the fact that several species of domestic animals with markedly different body sizes and lifespans all had lifetime basal energy expenditure of about

200 kilocalories per gram. The evidence adduced by Rubner was essentially that in Table I. The lifespans he attributed to some species in the table are out of line with currently accepted values, and introduction of the more accurate values would considerably weaken his evidence.

Although Rubner's own evidence is hardly adequate to support his thesis, the results of the present analysis indicate that his conjecture nevertheless has considerable merit. His hypothesis may be reformulated to say that the lifespan of a species varies inversely as its basal metabolic rate or, in the notation employed above,

$$x = -1{\cdot}00m + \text{constant} \tag{11}$$

Equation (10) shows, however, that the empirical relation between these variables is numerically

$$x = -0{\cdot}75m + \text{constant} \tag{12}$$

The significance of the difference between the theoretical and observed coefficients cannot be tested rigorously, so we cannot say whether this difference is in fact significant. However, Rubner's hypothesis that lifespan varies inversely as the first power of the metabolic rate is in any event subject to quantitative revision, for he considered only the basal metabolic energy. There is no good reason to distinguish between the resting and active energy expenditure with respect to their effects on length of life. Furthermore, the relation of active energy expenditure to body size is not accurately known. Hence, it can only be concluded at present that the empirical findings are in accord with the general hypothesis that the attainable length of life of a mammalian species is dependent in part on its rate of energy dissipation.

Rubner's original discussion of the energetic theory called attention to the fact that the lifetime energy expenditure for man is seriously out of line with the values calculated for domestic animals (Table I). This discrepancy was in fact one of the considerations that inspired me to undertake this

Table I

Lifetime energy expenditure (cal./g.) for several species of domestic animals and man (from Rubner, 1908)

Species	*Body Wt.*	*Length of life*	*Lifetime energy expenditure*
	kg.	(years)	(cal./g.)
Horse	450	30	170,000
Cow	450	26	141,000
Dog	22	9	164,000
Cat	3	8	224,000
Guinea pig	0·6	6	266,000
Man	70	100	800,000

allometric analysis. I had been working on a theory of mortality and ageing which took particular cognizance of the rôle played by physiological fluctuations (Sacher, 1956, 1958). The essential points of this theory are:

(a) mortality is essentially a random process in that the circumstances leading to death in an individual case cannot be predicted with certainty;

(b) the physical basis for this uncertainty is to be found in the fluctuations of physiological state that are inevitably present in living systems; and

(c) the magnitude of the physiological fluctuations is determined by the interplay between the random impinging disturbances (of external and internal origin) and the regulatory mechanisms that act to limit the magnitude and duration of their effects on the organism.

A central problem in the mathematical development of the theory is that of deriving the quantitative dependence of the probability of mortality in given circumstances on the parameters of the physiological fluctuation process. The important implication of the theory in the present context is that the attainable length of life for a species depends on the precision of physiological regulation that the species is capable of. The logical or mathematical developments that lead to this

inference will not be discussed, because in qualitative terms it is readily evident, and a quantitative mathematical statement is not testable at present owing to lack of appropriate data on precision of physiological regulations in different species.

In the absence of data that would permit a direct comparison of theory with experiment it was finally resolved to approach the problem indirectly, by introducing the mediating assumption that the precision of physiological regulation is directly related to the degree of encephalization. Several lines of published evidence suggested that such an approach might be fruitful. First, there was the great discrepancy between the human lifespan and that of other species, and also Rubner's statement about the discrepancy between man and other mammals in lifetime energy expenditure (see above). Second, Flower's tabulation of lifespans of mammals brought out the important point that man's long lifespan relative to that of other mammals is not unique, for primate species in general live longer than non-primates (Flower, 1931). Finally, there was the massive literature on the index of cephalization which indicated that this varies over wide limits (von Bonin, 1937), thus making possible an evaluation of the contribution of brain weight independent of body weight.

The statistical analysis presented above strongly supports the hypothesis that lifespan is specifically related to brain development. To establish my thesis completely I should next justify the mediating assumption that the overall precision of physiological regulations is governed by the central nervous system. To do so would take me far beyond the bounds of this paper, for it would entail a review of the vast and rapidly increasing literature on the control of vital physiological functions by the central nervous system, and by the cerebral cortex in particular (*Ciba Found. Symp. Neurological Basis of Behaviour*, 1958). The developments of the last few years have done much to dispel the dichotomy between "higher" and "lower" forms of behaviour in so far as their representation in the nervous system is concerned, and we

tend more and more to the view that the central nervous system participates in the vegetative processes continually. I therefore conclude that my assumption about the close relation between brain development and overall precision of physiological regulation is justified by our present knowledge. Moreover, I am confident that this relation will find concrete support when a quantitative comparative physiology comes into being which will make possible direct tests of more specific forms of this general assumption.

Identification of the factors which determine the characteristic ageing rates, and hence the lifespans of mammalian species, is one of the central problems of gerontology. In recent years several authors have proposed theories of ageing which posit a relation of ageing to the spontaneous mutation rate (Szilard, 1959) or to loss of information content (Yockey, 1958). Whatever other utility these theories may have, they contribute little to our understanding of ageing, for their authors fail to grasp the essential point that the spontaneous mutation rate and the ageing rate are concomitant species characters, so that to account for one in terms of the other is merely to restate an observed fact. It would undoubtedly be widely acknowledged that ageing must ultimately be accounted for in terms of irreversible alterations in the molecular make-up of organisms, and that gene mutations are an especially important class of such irreversible molecular changes. Given this consensus, the basic question is: *why* does the species mutation rate tend to be proportional to the mean death rate, or inversely proportional to the lifespan? I shall next discuss this question in the light of the energy dissipation and fluctuation hypotheses.

The occurrence of irreversible molecular changes in biological systems can be exhaustively discussed under four headings, as follows:

(a) thermal denaturation—alterations of molecular structure that are essentially due to thermal energy, and occur at a rate that is primarily dependent on the temperature;

(b) errors of synthesis and denaturations that occur in the steady state of metabolic activity—the probability of producing incorrect molecules per unit time arising from inherent imperfections of the metabolic process (inadequate specificity of enzymes, presence of by-product metabolic poisons, etc.) in the ideal steady state for the species as this is established by natural selection operating on the genetically controllable thermodynamic properties of enzymes;

(c) errors in synthesis and denaturations occurring as a result of deviations from the steady state;

(d) adventitious poisoning of environmental origin—radiation, poisons, etc. (this class will not be discussed here).

These classes of determiners are distinguishable by the way in which the observed ageing rate (mutation rate, etc.) depends on certain environmental and system variables. Thermal inactivation would operate equally on almost all mammalian species since they have (except for bats and some other forms) essentially the same constant body temperature. Thus thermal denaturation can be ruled out as a factor determining the different rates of ageing in different species. The error rate in the metabolic steady state should have a direct, essentially proportional relation to metabolic rate and in consequence a determinate relation to body mass. Hence, if this is an important factor in determining the rate of accumulation of ageing events one would expect lifespan to vary as an inverse function of metabolic rate. This is the Rubner hypothesis, which was seen above to be in general accord with the data.

The error rate due to fluctuations away from the steady state would tend to be smaller in species possessing superior physiological regulatory mechanisms, for in these species the mean square deviation from the steady state is smaller. The evidence on this point, deriving from the relation of lifespan to index of cephalization, is indirect but nevertheless persuasive, as was discussed earlier.

Thus the comparative, allometric approach has shown us

that the rate of accretion of ageing injury in mammalian species increases as the metabolic rate increases and decreases as precision of physiological regulation increases. Therefore the irreversible changes that underlie ageing are not necessarily and inevitably determined by the rate of dissipation of energy. The intervention of improved physiological regulations, by maintaining the average value of the *milieu intérieur* nearer to the biochemically ideal, and by reducing the magnitude of the fluctuations away from this average, acts to reduce the probability per unit time of irreversible changes, and thus to reduce the rate of ageing. This has been a highly significant feature in the evolution of mammals, and it remains to be seen whether man can take conscious advantage of this principle to bring about a real decrease in his rate of ageing.

Appendix 1. Relation of log lifespan to log body weight, log brain weight, index of cephalization and log specific metabolic rate. Also mean values, variances, and standard errors of the coefficients*.

a. Mean values and standard errors of the variables, and their variances.

Log lifespan (years)	$\bar{x} = 1{\cdot}283 \pm {\cdot}042$	$S_x^2 = {\cdot}10900$
Log body weight (grams)	$\bar{y} = 4{\cdot}099 \pm {\cdot}163$	$S_y^2 = 1{\cdot}67158$
Log brain weight (grams)	$\bar{z} = 1{\cdot}841 \pm {\cdot}113$	$S_z^2 = {\cdot}80666$
Index of cephalization	$\bar{w} = 0 \pm {\cdot}032$	$S_w^2 = {\cdot}06570$

b. Log lifespan (x) on log body weight (y). See Equation (2).

$$b_{xy} = {\cdot}198 \pm {\cdot}021 \qquad S_{x.y}^2 = {\cdot}04402$$

* The total regression of variable x on variable y is denoted by b_{xy}. The corresponding regression equation is

$$x - \bar{x} = b_{xy}(y - \bar{y})$$

The *partial* regression of x on y, independent of the regressions of x and y on a third variable, z, is denoted by $b_{xy.z}$. The multiple regression equation is of the form

$$x - \bar{x} = b_{xy.z}(y - \bar{y}) + b_{xy.z}(z - \bar{z})$$

The total variance of variable x is denoted by S_x^2. The variance of x that is not accounted for by regression on the other variable or variables in the regression equation is denoted by $S_{x.y}^2$, $S_{x.yz}^2$, etc.

c. Log lifespan (x) on log brain weight (z). See Equation (3).

$$b_{xz} = \cdot 325 \pm \cdot 022 \qquad S^2_{x.z} = \cdot 02403$$

d. Log lifespan (x) on log body weight (y) *and* log brain weight (z). See Equation (4).

$$b_{xy.z} = -\cdot 225 \pm \cdot 045$$

$$S^2_{x.yz} = \cdot 01730$$

$$b_{xz.y} = \cdot 636 \pm \cdot 065$$

e. Log brain weight (z) on log body weight (y); definition of index of cephalization (w). See Equations (5) and (6).

$$b_{zy} = \cdot 666 \pm \cdot 025 \qquad S^2_{z.y} = \cdot 06678$$

$$w = z - \cdot 666y + 0 \cdot 888$$

f. Log lifespan (x) on index of cephalization (w). See Equation (7).

$$b_{xw} = \cdot 636 \pm \cdot 143 \qquad S^2_{x.w} = \cdot 08381$$

g. Log lifespan (x) on log body weight (y) *and* index of cephalization (w). See Equation (8).

$$b_{xy.w} = \cdot 198 \pm \cdot 013$$

$$S^2_{x.yw} = \cdot 01730$$

$$b_{xw.y} = \cdot 636 \pm \cdot 065$$

h. Relation of log specific metabolic rate (m) to log body weight (y) as given by Brody (1945); regression of log lifespan (x) on index of cephalization (w) *and* log specific metabolic rate (m). See Equations (9) and (10).

$$m = -\cdot 266y + 1 \cdot 047$$

$$b_{xw.m} = \cdot 636 \qquad b_{xm.w} = -\cdot 745$$

REFERENCES

BONIN, G. VON (1937). *J. gen. Psychol.*, **16**, 379.

BOURLIÈRE, F. (1946). *Année biol.*, **22**, 249.

BRODY, S. (1945). Bioenergetics and Growth. New York: Reinhold Publishing Co.

Ciba Found. Symp. Neurological Basis of Behaviour (1958). London: Churchill.

COMFORT, A. (1956). The Biology of Senescence. New York: Rinehart.

COMFORT, A. (1958). *J. Geront.*, **13**, 342.

COUNT, E. W. (1947). *Ann. N.Y. Acad. Sci.*, **46**, 993.

DUBOIS, E. (1924). *Proc. kon. med. Akad. Wet.*, **27**, 430.

FLOWER, S. (1931). *Proc. zool. Soc. Lond.*, 145.

GUMBEL, E. J. (1958). Statistics of Extremes. New York: Columbia University Press.

Hald, A. (1952). Statistical Theory with Engineering Applications. New York: John Wiley and Sons.
Quiring, D. P. (1950). Functional Anatomy of Vertebrates. New York: McGraw-Hill.
Rubner, M. (1908). Das Problem der Lebensdauer und seine Beziehungen zurn Wachstum und Ernährung. Münich: Oldenbourg.
Sacher, G. A. (1956). *Radiology*, **67**, 250.
Sacher, G. A. (1957). *Anat. Rec.*, **128**, 616.
Sacher, G. A. (1958). *In* Symposium on Information Theory in Biology, ed. Yockey, H. P., *et al.*, p. 317. London and New York: Pergamon Press.
Szilard, L. (1959). *Proc. nat. Acad. Sci. (Wash.)*, **45**, 30.
Walker, E. P. (1954). The Monkey Book. New York: Macmillan.
Yerkes, R., and Yerkes, A. (1929). The Great Apes. New Haven: Yale University Press.
Yockey, H. P. (1958). *In* Symposium on Information Theory in Biology, ed. Yockey, H. P., *et al.*, p. 297. London and New York: Pergamon Press.

DISCUSSION

Danielli: The simplest physical interpretation of your regression equation, Mr. Sacher, is that it is an advantage to have a brain, and a disadvantage to have a body !

Wigglesworth: Barcroft's thesis (Barcroft, J. (1934). Features of the Architecture of Physiological Function. Cambridge University Press) was that a constant internal environment was primarily essential for the functioning of the brain, and that for higher development of the brain you needed a more constantly regulated internal environment. As I understand your theory, that same constancy will also be favourable to longevity, so that cephalization and longevity should go hand in hand.

Verzár: Do you not think that lifespan as a measurement of ageing trends is a bad measurement, Mr. Sacher ? Lifespan is the most uncertain of all our records. The mortality curves are not straight ; they are always an "S" shape, and the right side of that "S" shape, especially, is extremely long, so that exceptionally long lives are particularly noticed. Wouldn't it be much better to relate all our age theories not to the maximal lifespan, but to something like a 50 per cent survival of a certain population ? That would make the whole thing experimentally much more certain.

Sacher: I agree that maximum lifespan is a gross measure. That it is a bad measure I would not agree. Lifespan is an extremum statistic, and can be handled in a perfectly rigorous fashion by statistical

reasoning, as is shown in Gumbel's treatise (1958). Moreover, life expectations or the median survival times are available for only about six of the 100 or so species that ideally we would like to use in this sort of comparative analysis. Finally, as I pointed out in my paper, maximum lifespan is a better estimator of the intrinsic ageing characteristics of the population than is the median or average survival. However, I do not advocate its use in the analysis of laboratory data, or in any situation where life-tables are available.

Incidentally, I have been concerned about the problem of what is proper to use as a lifespan for man. Zoo animals are not kept under ideal conditions, as they get little individual attention or medical care. Therefore perhaps some earlier state of human culture would be more comparable. It is interesting that you can get data on the ages of fossil skulls back to the Palaeolithic (Vallois, H. V. (1937). *Anthropologie, Paris*, **47**, 499; Weidenreich, F. (1939). *Chin. med. J.*, **55**, 34). Peking man, in a sample of only six skulls, yielded one that probably had an age of over 50 years. They lived under far poorer conditions than our zoo animals today. Neolithic man lived to more than 70 years, even according to rather small samples.

Comfort: I think you have been taking much more plausible maximum ages than Rubner did, Mr. Sacher. Rubner gave the life-span of a dog as nine years and of a cat as eight years, which is quite arbitrary. Cats can quite possibly live for 30 years and the extreme credible record for a dog is between 20 and 25. There are much greater discrepancies between the modal and maximum records for animals, and the acceptable mode and maximum for man. I think most people would agree that 110 to 120 is the extreme limit for which there is any good evidence in man, in spite of the 140-year-old Russians. Most cats die before they are 16, but a few have lived very nearly twice that time. One has also to beware among animals of the possibility of very long-lived genotypes and of the differences between hybrid and inbred strains.

Sacher: The extreme error in the individual lifespan records is probably a factor of 2 or so, but if the errors are random, their only effect is to weaken the degree of order observed.

Holt: Have you looked at data for aquatic mammals ? They have some exceptionally large body sizes, without corresponding increases in brain size, and there are many published age determinations for them, but perhaps not maximum lifespans.

Sacher: When I did this work I did not have enough data on aquatic mammals, but I want to study them in future.

Maynard Smith: There is a possibility of bias in estimates of this kind since most of the small mammals in your sample are rodents,

and most of the large ones are ungulates. It would be interesting to know whether, if you calculate your coefficients just on rodents, just on primates, and just on ungulates, you would get results which are at least approximately consistent with those you get on the whole sample combined.

Sacher: I only know this qualitatively and graphically. The values of the allometric coefficients vary considerably from order to order. The goodness of fit would have been greatly improved if I had omitted the ungulates, because they have quite different allometric relations of body weight to brain weight, and in effect they made the overall relation poorer.

Rotblat: I was very glad to see that you describe life processes in terms of numbers. I was a little bit disturbed, however, when you ended up by introducing a term which cannot be expressed in numbers, namely stability or adaptability of physiological function. Can you put this in some kind of quantitative relation to the index of cephalization, or the mitotic activity ? Have you any indication that there may be some ways of increasing lifespan by increasing stability ?

Sacher: The term "stability" in my thinking is a general term that subsumes all the properties that have to do with mortality, stress resistance, length of life, etc. In this sense, an animal that lives longer has greater stability, and a species that has a lower mortality rate for a given disease or stress has greater stability. In other words, stability is a general physical character of organisms. If one holds the point of view that all these things are fated, determined in advance by the genotype, then there is no reason for talking about stability. But if one thinks of organisms as dynamic functioning systems whose probabilities of failure arise from their function (Sacher, 1956, 1958), then stability is a natural term and it becomes reasonable to think of improving the stability characteristic of organisms. We cannot replace any of our bodily elements with better ones, as an engineer can replace vacuum tubes, but it might be possible (remembering that the central nervous system is implicated in every physiological activity, and that these responses are conditionable) eventually to evolve a kind of ontogeny and conditioning that would make for more stable physiological functioning in the given environment.

Rotblat: This seems to be going around in circles. You have explained the span of life in terms of stability and *vice versa.* It seems to me that mutation rate is a quantity outside the circle, because you can say that there is something which goes on all the time independently of us.

Sacher: If mutations are considered to be molecular events, then one has to ask why the molecules in the mouse mutate some thirty times faster per unit time than they do in man. I have shown that two physical characteristics of mammals, namely the metabolic rate and the goodness of physiological regulation, account for most of the lifespan variance. Some fraction of the remaining variance is undoubtedly under specific genotypic control, but this is a small part of the total. Thus it would appear to be true that species tend to have the maximum attainable lifetimes permitted by their body size and complexity of organization.

Danielli: You suggested that there might be a standard amount of metabolism which was permissible per gram of tissue before it deteriorated beyond hope. Could any information about this be obtained, perhaps in fish, by using a poison such as dinitrophenol, which causes a good deal of useless metabolism to go on ? This might enable one either to discover that the life expectancy was a function of the amount of oxygen utilized in respiratory processes, or else to distinguish between one type of metabolism which has an ageing effect, and other types of metabolism which have not. It is probably easier to keep up a constant concentration of dinitrophenol in fish than it is in many other animals.

Sacher: I have not yet had the opportunity to do such experiments; it would certainly be extremely productive to use metabolic poisons. In warm-blooded mammals one also could replace part of the basal energy production by producing heat internally with radiofrequency heating. Anything that would produce a dissociation between the amount of metabolism and the other physical characteristics of the organism would be extremely valuable.

I would also like to determine whether one could systematically yet diffusely decrease the general regulatory ability, perhaps by destroying the brain to a certain degree, with sonic radiation or diathermy. Can anyone suggest how a uniform controllable deterioration could be produced which could be followed in terms of its effect on survival ?

Lindop: Could one use colchicine as a mitotic inhibitor in different doses ?

Danielli: It might have some effect, but I should have thought it might be better if you could use something of the nature of a cholinesterase inhibitor, or strychnine.

Comfort: An experiment with dinitrophenol was done upon mice by M. L. Tainter (1936. *Proc. Soc. exp. Biol.* (*N.Y.*), **31**, 1161). Mice treated over a period of time did not seem to have their lifespan very much affected—certainly not in proportion to their metabolic rate.

Danielli: That would definitely mean that it was not just a respiration effect.

Comfort: With many of these animals you may increase their metabolism and at the same time decrease their appetite, or something like that. One has to be careful.

Sacher: If it did not have any effect on body temperature it would not greatly increase the overall metabolism would it ?

Comfort: I do not know whether there was that effect or not—the paper may say.

Danielli: Dinitrophenol would normally increase the metabolism a lot, unless there were some compensatory mechanisms, and one would expect appetite to increase rather than diminish.

Bourlière: Long ago T. B. Robertson (1928. *Aust. J. exp. Biol. med. Sci.*, **5**, 69) found that continuous treatment of the mouse with desiccated thyroid, in quantities that stimulated growth, also shortened the lifespan.

Berg: We are studying the effect of thyroidectomy on the lifespan of the rat.

Maynard Smith: Another possible way of studying the effects of metabolic rate on longevity is to use different genetic strains of the same species. The most striking differences in longevity you can get in flies are between inbred and outbred; outbred flies will live about twice as long as inbred ones. This certainly is not associated with a lower rate of metabolism in the outbred flies. They are not animals in which it is easy to measure the basal metabolic rate, but if one judges it by rate of egg production, for example, the hybrids are laying eggs at about twice the rate of the inbreds, as well as living twice as long. Also the hybrids are much more active. Their greater longevity is much more easily explained in terms of the other concept that Sacher used, namely that the hybrids in many respects, both physiologically and developmentally, seem to have far better stabilizing mechanisms than do inbreds, and that what is wrong with inbred animals is that they are just not good at regulating against anything.

Sacher: Yes, that is a view which is put forward systematically in the concept of genetic homeostasis.

Maynard Smith: I think it is a true one.

Sacher: In general terms I think it is true also. We have the same phenomenon in mice but not to the same degree.

Verzár: Thyroxine treatment of the tadpole and axolotl, which—as you know—leads to transformation from larval to adult forms, always leads to a shortening of life. The transformed animals never survive long.

Nigrelli: Is that true of well-fed and of starved tadpoles ? Well-fed tadpoles should not metamorphose as rapidly as starved ones.

Verzár: In the cases which I know of the tadpoles were well fed.

Lindop: Mr. Sacher, you were trying to put something forward mathematically, using your concept of lifespan. I tried to relate your criterion to what we were doing, and I found that I could not apply it. In a discussion group like this, where there are so many different disciplines, and we are each putting forward our own specialist information, a short discussion on what is the most useful concept of lifespan for us to be able to compare our different groups might be helpful. People who have experiments which are half-way through would then know what others want them to do for the rest of them.

Can you use your mathematical interpretations to get a mathematical correlation between lifespan in naturally occurring populations and in populations where we have altered the lifespan ? By irradiation we have altered lifespans both by your definition and ours, but we have not changed the index of cephalization.

Sacher: There are certainly many factors affecting length of life. The thing has to be put into perspective. I have used the lifespan I defined above—the maximum attained life—only in the present context of doing a comparative study on a very broad scale. When I am working on laboratory data I usually use the life expectation, and specifically the after-expectation of life from the beginning of exposure. In order to characterize the effects of radiations on populations, we have found that it is particularly convenient to discuss these in terms of the log rate of mortality (Gompertz) curve (Sacher, 1956; Brues A. M., and Sacher, G. A. (1952). *In* Symposium on Radiobiology, ed. Nickson, J. J., p. 441. New York: John Wiley). Before discussing this I wish to point out that any one of the life-table functions contains the same amount of statistical information as any other, as long as you have not lost information by rounding, setting up large class intervals, etc. The reason for preferring some particular analytical function of the basic data is that it seems to give the clearest insight into underlying mechanisms.

Cohorts of mice kept under laboratory conditions have life-tables such that the plot of logarithm of rate of mortality (Gompertz transform) either is a straight line or shows a moderate amount of curvature. In various mouse strains, the slope of the best-fitting straight line at advanced ages (omitting the mortality primarily due to infectious disease in young mice) does not vary significantly. In hybrids showing marked hybrid vigour the slope again remains unchanged, and the increased survival is due to a decrease in the

intercept values. A single dose of X-rays given in early adult life is followed, after a latent period of 100–200 days, by a displacement of the Gompertz transform parallel to itself (Fig. 1). In cases where the Gompertz transform shows some curvature, it is possible to infer that this displacement is a translation to the left on the time axis. The interpretation is that the Gompertz transform is a linear measure of the amount of ageing injury present. A single X-ray dose produces a residue of permanent injury, and this is manifested by a displacement of the Gompertz transform by a constant amount.

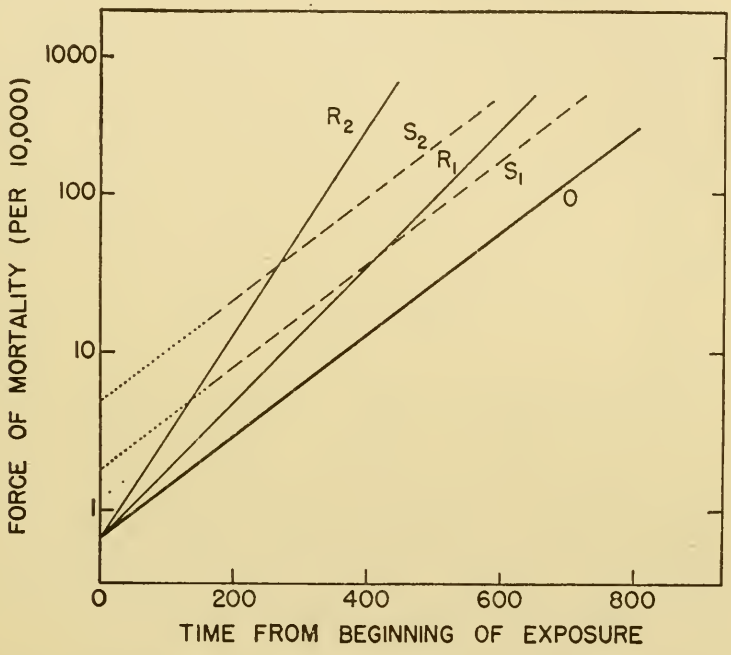


FIG. 1 (Sacher). Schematic representation of the long-term effect of single or repeated exposure to ionizing radiations on the Gompertz function (logarithm of the age-specific rate of mortality) for mammals. The age-trend of mortality is considered to conform to the Gompertz *equation* (compare with equation 1 and text)

$$\log\left(\frac{1}{N}\frac{dN}{dt}\right) = \log A + \alpha x$$

where N is the number living at age x.
O—unirradiated population; S_1, S_2,—populations given single exposures at time zero; R_1, R_2—populations given repeated or continuous exposure beginning at time zero. Early portion of lines S_1 and S_2 dotted to indicate time needed for displacement to attain its steady value.

If each X-ray dose produced a constant displacement of the Gompertz function, and if they added with one another as well as with the basic ageing trend, then a cohort exposed daily throughout adult life should show a constant divergence from controls, and a set of different daily doses should produce a fan of Gompertz curves. This is in fact seen (Sacher, 1956). The parameters of the daily dose response are consistent with those of the single dose response.

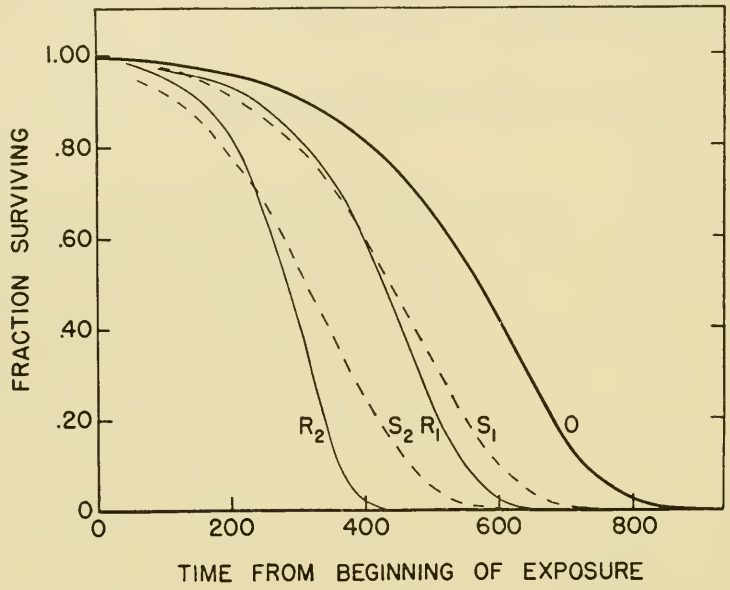


FIG. 2 (Sacher). Survivorship curves corresponding to the schematic Gompertz functions in Fig. 1. The "single dose" curves can be superimposed on the "control" curve by sliding them to the right. The "repeated exposure" curves can be superimposed on the "control" by multiplications of their time scales by scaling factors.

This mode of analysis therefore gives a parsimonious description of radiation mortality, and relates it to the ageing process in terms of a life-table function, the Gompertz function, where properties are consistent with the hypothesis that the function is a linear measure of the amount of ageing injury present in the population. A theoretical justification of this hypothesis can be given in terms of the concepts of physiological fluctuations and probability of failure that were introduced in the text (Sacher, 1956).

In view of the earlier point, that any one of the life-table functions contains the same information as the others, it follows that any other desired quantities, such as expectations, medians, deciles,

etc., can be computed in turn. My chief concern was to validate a theory of radiation mortality and ageing. However, empirical analysis and theoretical analysis should have the same goals of parsimonious description. Thus the Gompertz function, which is a theoretically meaningful one, should also be best for empirical analysis.

Verzár: Could you describe the same thing with survival curves, Mr. Sacher ?

Sacher: An animal following a single radiation dose acts at a given age like a control animal at somewhat greater age. The irradiated population tends to show shallower survivorship curves which can be translated and scaled so that they can be superimposed on a control population of a later starting age (Fig. 2). This can be accomplished without changing the time scale, and corresponds to the fact that single X-ray doses displace the Gompertz function parallel to itself without change of slope. If we give daily doses of irradiation, the effect is not as if we had set the clock forward but rather as if we had changed the regulator, so that the clock runs faster. Thus, concomitant with the decrease in survival time there is a steepening of the survival curve in the daily dose condition. That corresponds to the fan of lines on the log rate of mortality plot.

Maynard Smith: In comparing life-tables based on wild populations and on laboratory populations, I think what both Dr. Comfort and Mr. Sacher have had in mind here is that what such distributions are most likely to have in common is the maximum lifespan; the oldest individuals in wild populations may correspond roughly in age to the oldest individuals in laboratory populations, but the two distributions have little else in common.

Sacher: I can agree with that. It is not yet possible to reach a meaningful correlation between life-tables in the field, and life-tables in controlled environments. These conditions are so far apart that we cannot discuss the respective life-tables in terms of common parameters. It would seem that there have to be intermediate grades of environment between the wild and the laboratory.

Lindop: Is there any one method of investigation in which, instead of going through the changes gradually, we could correlate them more rapidly ? For instance, one might take the causes of death in wild animals and the causes of death in laboratory animals, exclude from each group the causes which are not in common, and see how the survival curves fitted for the causes of death which are in common.

Sacher: That certainly could be done if they had enough causes of death in common.

A REVIEW OF THE LIFESPANS AND MORTALITY RATES OF FISH IN NATURE, AND THEIR RELATION TO GROWTH AND OTHER PHYSIOLOGICAL CHARACTERISTICS

R. J. H. Beverton and S. J. Holt

Ministry of Agriculture, Fisheries and Food, Fisheries Laboratory, Lowestoft; and Fisheries Biology Branch, F.A.O., Rome

Studies on the dynamics of fish populations have received a major impetus in recent years owing to the need to provide an adequate scientific basis for conservation. One aspect of these studies is the measurement of fish longevity and the force of natural mortality in fish populations. In this contribution we attempt to review the present state of knowledge on these questions.

In so doing we have two objectives in mind. One is to present the data on longevity and mortality in fish for comparison with what is known for other animals and presented at this symposium; the other is to see to what extent these characteristics are, in fish, associated with size, growth, maturation and certain other physiological factors for which data are available.

It has not been possible for us to search through the widely scattered literature as thoroughly as we would have wished. The paper is therefore perhaps best regarded as a progress report from which certain tentative conclusions can be drawn at this stage.

Natural mortality and lifespan

Many of the fish populations which have been intensively studied are those supporting a major commercial fishery and are therefore ones in which the effect of fishing has profoundly

influenced the shape of the survival curves and the maximum age recorded in samples. There are, nevertheless, a certain number of instances in which the natural age composition, or

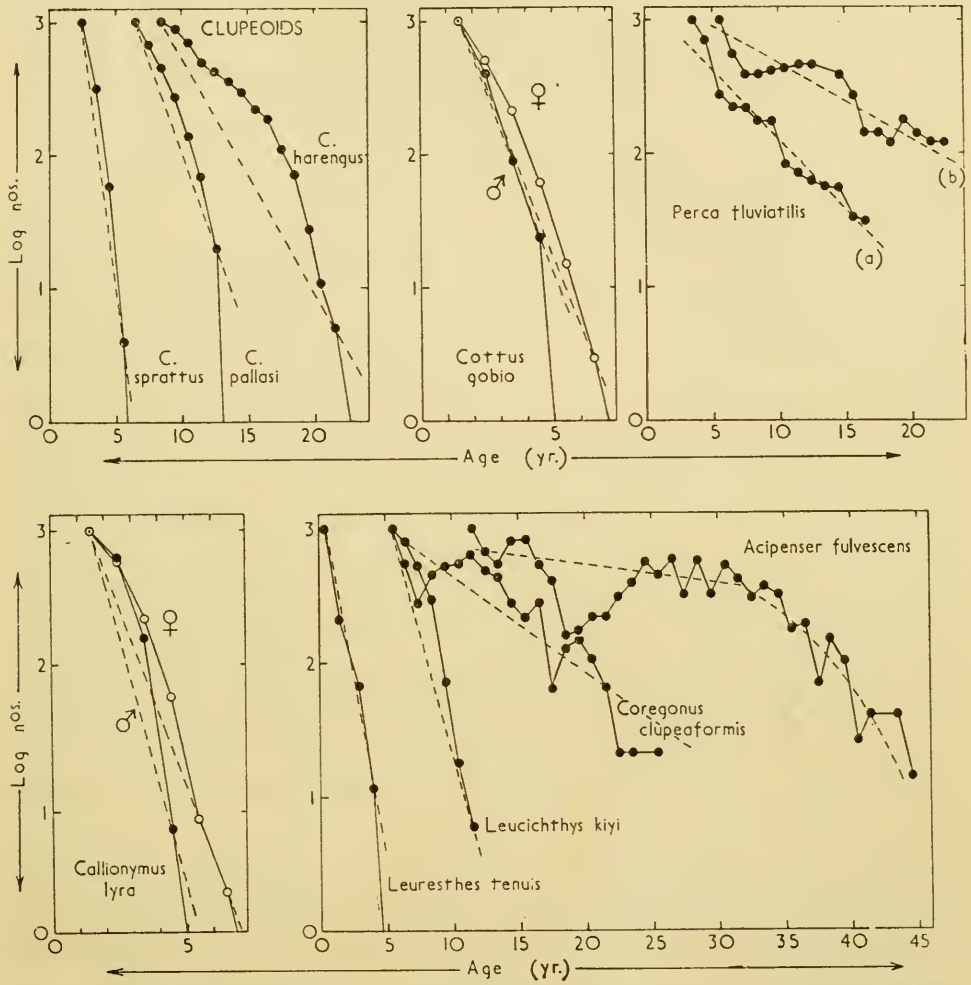


FIG. 1. Some examples of survival curves in relatively unexploited fish populations.

something fairly close to it, has been determined, and some examples of these are shown in Fig. 1. It will be noted that in no case do the data cover the whole lifespan from birth onwards; this is because representative sampling of the fry and

juveniles is seldom possible. It is known, however, that in many species, and especially in those which lay large numbers of eggs, there is a very high mortality during the first weeks of life; in North Sea plaice, for example, only about one in ten thousand survive the first few months. Thus the survival curve for fish characteristically descends very rapidly at first and then flattens out, though in viviparous species, and species which lay a small number of eggs but afford the newly-hatched fry some degree of parental care, this initial descent is probably less marked.

Even after the early phase of heavy mortality some considerable time may elapse before the fish have grown large enough to be retained by the fishing gear, so that a representative survival curve has to begin at some later age when the individuals are first properly represented in the samples. The survival curves shown in Fig. 1 therefore start at the age group which is most abundant in catches, and for comparison all the data have been adjusted to a peak number of 1,000. The numbers are plotted on a logarithmic scale, so that a linear survival curve indicates a constant natural mortality rate independent of age, whereas a downward curve shows that the mortality rate is increasing with age. The broken lines are drawn purely to assist the eye in detecting linearity or departures from it, and where the survival curve is not a straight line the broken lines are drawn through the first and last points.

In the long-lived species, of which the examples shown in Fig. 1 are sturgeon (*Acipenser fulvescens*; Probst and Cooper, 1954), whitefish (*Coregonus clupeaformis*; Hart, 1931) and perch (*Perca fluviatilis*; Alm, 1952), the mortality rate seems to be effectively constant over a considerable span of age at about 5 to 10 per cent per year, although in the age groups of sturgeon beyond about 30 years the mortality rate appears to increase. The fluctuations in the data for sturgeon and whitefish are partly due to the fact that sampling was possible for a limited period only and that the age groups refer to

different year classes of fish whose initial abundance varies considerably. The perch data are unique because they show the survival of a known number of fish introduced into experimental ponds—in the one case as fry (*a*) and in the other as five-year-old fish (*b*)—and then sampled regularly for 15 years and 17 years respectively; within these spans of age there is no evidence of a varying age-specific mortality rate.

Of the shorter-lived species shown in Fig. 1, nearly all have a survival curve with some degree of downward curvature over nearly the whole range. This is seen particularly clearly in the herring data (*Clupea* spp.), of which those for the Norwegian herring (*C. harengus*; Lea, 1930) are the combined data for a period of twenty years in which year-class fluctuation has been largely eliminated. The data for the bullhead (*Cottus gobio*; Smyly, 1957) and the dragonet (*Callionymus lyra*; Chang, 1951) are included to show the difference between the survival curves for males and females. In both of these the males have a higher mortality rate and a shorter lifespan, and this is indeed what is usually found where there is any difference between the sexes; we have, however, come across one or two exceptions which are referred to later.

The tendency for the natural mortality rate to increase with age, which is noticeable in several of the examples shown in Fig. 1, is, indeed, found more often than not, and for other instances the reader is referred to papers by, for example, Kennedy (1954) on the Lake trout (*Cristivomer namaycush*), by Wohlschlag (1954*a*) on the Alaskan whitefish (*Leucichthys sardinella*), and by Ricker (1949) on several species. This variation of the mortality rate with age reaches an extreme form in species where all or nearly all individuals die at, or soon after, spawning for the first time. The best known instance of this is in the Pacific salmon (*Oncorhynchus* spp.), which migrates up-river from the sea at between three and five years of age, spawns and then dies. The immature phase of the life-cycle spent in the sea has only recently been studied,

but there is no reason to believe that the mortality rate during that time is abnormally high. Other examples of a catastrophic mortality at, or shortly after spawning include the Tasmanian whitebait (*Lovettia seali*; Blackburn, 1950); the capelin (*Mallotus villosus*; Templeman, 1948); the small freshwater atherinid *Labidesthes sicculus* (Hubbs, 1921) which spawns at about one year of age and then dies off within a further two or three months; and, probably, the dragonet (*Callionymus lyra*; Chang, 1951). In most of these it is the males which suffer the most severe mortality, the evidence being that a proportion of the females spawn more than once, even though that proportion may be small.

Survival curves in fish thus range from effective linearity over the whole of the observed range of age to sharp discontinuity at the onset of maturity, with a wide range of intermediates in which the mortality rate increases steadily with age without obvious discontinuity. This makes it difficult to adopt any single numerical index as an index of lifespan, or of force of mortality, for all species. Thus the maximum age recorded in samples is satisfactory for the species in which the mortality rate increases fairly sharply with age, but is less so in the long-lived species, where it becomes rather critically dependent on the size of the samples and on the accuracy of the age-determination technique. Conversely, the average mortality rate is not a particularly useful measure where the mortality rate is highly age-specific, but is satisfactory in the long-lived species with nearly linear survival curves.

For the time being we have therefore tabulated wherever possible both the maximum age recorded in the sample (T_{max}) and the average instantaneous coefficient of natural mortality (M) over the range of age groups which, as far as we could judge, were fully represented in the same samples. These are given in Table I, from which it will be seen that the lifespan of fish can range from little more than a year in several quite unrelated species including *Labidesthes*, of the mullet family,

and *Lovettia seali* of the salmonoid family mentioned above, *Hypomesus olidus*, the pond smelt, another of the salmonoids, and the dwarf sea-horse (*Hippocampus hudsonius*), to over 80 years in the Lake sturgeon (*Acipenser fulvescens*). The maximum recorded age we have found is, in fact, for this latter species (Anonymous, 1954), a specimen 206 cm. long taken in an Ontario lake having been assigned an age of 152 years by examining the structure of the pectoral fin-ray. While it is quite possible that the precise age of such a fish cannot reliably be determined in this way, the work of a number of authors on the longevity of this and related species of sturgeon is consistent in showing that they can live to a great age, and it is indeed not unlikely that the occasional truly centenarian sturgeon is still to be found in the more remote water basins as yet untouched by man. Apart from sturgeon and the whitefish mentioned above, other long-lived species include the Arctic char (*Salvelinus alpinus*; Grainger, 1953) and the halibut (*Hippoglossus* spp.); whitefish and char are both salmonoids, but sturgeon and halibut are of different suborders, so that neither of the extremes of lifespan in fish are confined to a particular taxonomic group.

In compiling the data on maximum age in Table I we have not used the records for fish in captivity, of which a recent summary is included in the longevity data given by Brown (1957) and further data are presented to this colloquium by Nigrelli. There is nevertheless a broad agreement between the records from the two sources, and the few instances in which there is reason to believe that the entry in Table I may be substantially below the true maximum age of the species are noted in the legend to that Table.

Size and growth

Longevity and body sizes are known to be associated in higher vertebrates, especially in mammals (e.g. Sacher, this volume), so that it is of interest to see to what extent the same is true of fish. The growth cycle in fish is, however, more

Table I

COLLECTED DATA ON GROWTH, MORTALITY, LONGEVITY AND

Notes: (i) L_∞ and K are the parameters of the growth equation (1) given on p. 157, L_m = mean length at maturity.

(ii) In a few instances the value of T_{max} obtained from the age composition samples longevity of the same or closely related species in captivity, of which a recent sum- ages recorded by Brown are as follows: *Gadus virens*, 14 years; *Melanogrammus Dasyatis pastinaca*, 21 years.

Species	*Common Name*	*Locality*
Clupeoidei		
Clupea harengus	Atlantic herring	North Sea
C. harengus	Atlantic herring	Norwegian Sea
C. harengus	Atlantic herring	Lusterfjord (Norway)
C. harengus	Atlantic herring	New Brunswick
C. pallasii	Pacific herring	Canada (west coast)
C. sprattus	Sprat	North Sea
Sardinops caerulea	California sardine	California
S. neopilchardus	Australian sardine	Australasia
Gadiformes		
Boreogadus saida	—	Arctic Ocean
Gadus callarias	Cod	North Sea
G. callarias	Cod	Barents Sea
G. minutus	Poor cod	English Channel
G. minutus	Poor cod	Mediterranean
G. virens	Coalfish	Norwegian Sea
Melanogrammus aeglefinus	Haddock	North Sea
Merluccius merluccius	Hake	Marmora Sea
Pleuronectoidei		
Citharichthys sordidus	Sand dab	California
Hippoglossus vulgaris	Halibut	N. Atlantic

SIZE AT MATURITY OF FISH IN NATURAL POPULATIONS

M = natural mortality coefficient, T_{max} = maximum age recorded in samples,

(indicated by an asterisk) is somewhat below that recorded from records of the mary has been compiled by Brown (1957). For the fish in question, the maximum *aeglefinus*, 14–15 years; *Salmo trutta*, 18 years and more; *Anguilla anguilla*, 55 years;

Author	*Sex*	L_∞ (*cm.*)	K	M	T_{max} (*sample*)	L_m (*cm.*)	L_m/L_∞
Burd (unpub.)		30	0·38	0·25	12	24	0·80
Lea (1930) / Runnstrom (1936)		34	0·27	<0·2	22	28	0·82
Aasen (1952)		21	0·65	0·78	10	—	—
Tibbo (1957)		34	0·36	—	19	25	0·74
Tester (1937) / Ricker (1958)		23	0·29	0·56	11	—	—
Robertson (1938)		13	0·70	<1·2	5·5	10	0·77
Clark (1940) / Silliman (1943) / Phillips (1948) / Beverton & Holt (1957)		26	0·39	0·15	13	18·5	0·71
Blackburn (1950)		20·5	0·22	—	6·5	9(?)	0·44(?)
VNIRO (1949)		22	0·67	—	5	—	—
Beverton & Holt (1957) / Beverton (unpub.)		132	0·2	≃0·2	>11	—	—
Rollefsen (1954) / Taylor (1958)		134	0·1	—	23	85	0·64
Menon (1950)	m	20	0·42	1·1	5	11	0·55
	f	24	0·40	0·9	5	13	0·54
Vives & Suau (1956)		21	0·97	>2·3	2	—	—
Gottlieb (1957)		107	0·19	0·15	10*	71	0·66
Beverton & Holt (1957) / Raitt (1939)		53	0·20	>0·2	10*	26	0·49
Akyuz (1959)	m	44	0·13	0·6	10	23	0·52
	f	60	0·10	0·5	10	27	0·45
Arora (1951)	m	30	0·3	<0·3	7	—	—
	f	>30	<0·3		8	19	<0·63
Devold (1938)	m	170	0·04	—	30	95	0·56
	f	250	0·02	—	30	132	0·53

Table I—*continued*

Species	*Common Name*	*Locality*
H. stenolepis	Halibut	N. Pacific
Isopsetta isolepis	Butter sole	Canada (west coast)
Pleuronectes platessa	Plaice	North Sea
Pseudopleuronectes americanus	Winter flounder	Canada (east coast)
Solea vulgaris	Sole	North Sea
Salmonoidei		
Argentina semifaxiata	Argentine	Japan
Coregonus clupeaformis	Whitefish	L. Nipigon, Canada
C. clupeaformis	Whitefish	Shakespeare Is. Lake, Canada
C. clupeaformis	Whitefish	L. Opeongo, Canada
C. clupeaformis	Whitefish	Trout Lake, Wisconsin
C. clupeaformis	Dwarf Whitefish	L. Opeongo, Canada
Cristivomer namaycush	Lake Trout	Gt. Slave L., Canada
Hypomesus olidus	Pond smelt	L. Suwa, Japan
Leucichthys artedi	Cisco	Wisconsin, Trout Lake
		,, Muskellenge L.
		,, Silver L.
		,, Clear L.
L. kiyi	Chub	U.S.A.
L. sardinella	Whitefish	L. Ikroavik, Alaska Tasmania
Lovettia seali	Tasmanian whitebait	
Mallotus villosus	Capelin	Labrador
Oncorhynchus nerka	Sockeye salmon	Cultus L., Canada

Author	*Sex*	L_∞ (*cm.*)	K	M	T_{max} (*sample*)	L_m (*cm.*)	L_m/L_∞
Thompson & Herrington (1930); Thompson & Bell (1934)		Similar to *H. vulgaris*		<0·3			
Hart (1948)	m	38	0·36	<1·41	10	18	0·47
	f	42	0·26	<1·02	—	21	0·50
Beverton (unpub.)	m	45	0·15	0·22	13	25	0·56
	f	70	0·08	0·12	22	28	0·40
Dickie & McCracken (1955)		44	0·4	0·3	>10	32	0·73
Beverton & Holt (1957); Margetts (unpub.)		39	0·4	≃0·25	>8	—	—
Hanyu (1956)		19	1·2	—	2	—	—
Hart (1931)		50	0·13	0·17	24	≃27	≃0·55
Hart (1931)		49	0·09	0·15	27	≃27	≃0·55
Kennedy (1943)		70	0·06	<0·5	12	—	—
Hile & Deason (1934)		44	0·09	—	14	>23	>0·52
Kennedy (1943); Ricker (1949)		14	0·43	1·3	5	—	—
Kennedy (1954)		56	0·07	0·6	25	18·4	0·33
Shiraishi (1957); Sato (1950)		11–12	1·5–1·8	1·1–3·8	1–3	10	≃0·9
Hile (1936)	m	19	0·65	1·1	6	12·5	0·66
	f			1·1	11		
	m	21	0·36	1·2	3	15·0	0·72
	f			1·2	4		
	m	32	0·06	1·1	6	14·0	0·44
	f			0·9	7		
	m	39	0·27	0·4	9	13·0(?)	0·33(?)
	f			0·3	11		
Deason & Hile (1947)	m	28	0·51	<0·9	7	<18	<0·64
	f			<0·8	10		
Wohlschlag (1954*a*, *b*) (and personal comm.); Cohen (1954)		38	0·40	0·6	11	—	—
Blackburn (1950)		6–7	—	—	2	5(?)	0·8(?)
Templeman (1948)	m	20	0·48	1·3	5	18	0·90
	f	19	0·48		5	17	0·90
Foerster (1929)		69	0·58	—	6	60	0·87

TABLE I—*continued*

Species	*Common Name*	*Locality*
		Columbia R., Canada
O. keta	Chum salmon	4-year spawners
		3-year spawners
Salmo salar	Atlantic salmon	Scotland
S. trutta	Trout	L. Windermere, England
Salvelinus alpinus	Char	Baffin I., Canada
ACIPENSERIFORMES		
Acipenser fulvescens	Lake sturgeon	Wisconsin
A. { *medirostris* / *transmontanus*	White sturgeon	California
A. nudiventris	Sturgeon	Europe
ANGUILLOIDEI		
Anguilla anguilla	Eel	Windermere
BLENNIOIDEI		
Blennius pholis	Blenny	Welsh coast
CALLIONYMOIDEI		
Callionymus lyra	Dragonet	English Channel
COTTOIDEI		
Cottus gobio	Bullhead	Windermere
		R. Brathay
CYPRINODONTIFORMES		
Gambusia holbrookii	Top minnow	Portugal
CYPRINOIDEI		
Phoxinus phoxinus	Minnow	Windermere
GASTEROSTEIFORMES		
Gasteroteus aculeatus	3-spined stickleback	Cheshire
	10-spined stickleback	,,

Author	*Sex*	L_∞ (*cm.*)	K	M	T_{max} (*sample*)	L_m (*cm.*)	L_m/L_∞
Marr (1943)	m	120	0·27	(3·0)	5	81	0·68
	f	105	0·30			75	0·72
	m	106	0·45	(1·2)	5	75	0·72
	f	102	0·39			70	0·69
Nall (1927)		125	0·75	1·1(f)	6(f) 5(m)	—	—
Frost & Smyly (1952)		30	0·36	0·94	8*	24	0·75
Grainger (1953)	m	150	0·02	0·24	24+	—	—
	f	140	0·03	0·24	24+	60	0·43
Probst & Cooper (1954)		178	0·05	0·01	82	100–125	≃0·6
Pycha (1956)		300	0·06	0·03	30	100–125	≃0·4
Paccagnella (1948)		250	0·04	—	30	119–141	≃0·5
Frost (1945)	(Mostly f)	165	0·02	V. small	(17)*	60	0·37
Qasim (1957)		17	0·30	0·9	6	8	0·47
Chang (1951)	m	25·0	0·43	0·96	4	17·4	0·70
	f	17·5	0·55	0·86	6	—	—
Smyly (1957)	m	7·2	0·7	1·1	4	4·6	0·64
	f	7·3	0·4	0·9	6	4·2	0·58
	m	6·5	0·9	0·9	4	≃5	≃0·77
	f	6·5	0·5	0·8	6	≃5	≃0·77
Da Franca (1953)	m	3·6	1·2	<1·6	1	—	—
	f	6·2	0·8	<0·8	3	—	—
Frost (1943)		9	0·55	1·1	3	3·5–4	≃0·4
Jones & Hynes (1950)		6·7	0·64	0·9	4	3·6	0·54
		4·3	1·6	1·1	4	3·7	0·86

Table I—*continued*

Species	*Common Name*	*Locality*
Mugiloidei		
Leuresthes tenuis	California grunion	California
Labidesthes sicculus	Brook silverside	U.S.A.
Percoidei		
Cynoscion macdonaldi	Totoaba	Mexico
Perca fluviatilis	Perch	Sweden (a)
P. fluviatilis	Perch	Sweden (b)
Sillago sihama	Indian sand whiting	S. India
Stizostedion canadensis	Sauger	L. Nipigon, Canada
Rajiformes		
Dasyatis akajei	Ray	Japan
Scombroidei		
Rastrelliger neglectus	Chub mackerel	Gulf of Thailand
Pneumatophorus diego	Pacific mackerel	California
P. japonicus	Japanese mackerel	Japan
Siluroidei		
Ictalurus lacustris punctatus	Channel catfish	Mississippi R.
Syngnathiformes		
Hippocampus hudsonius	Sea horse	Florida
H. hudsonius	Pigmy sea horse	Florida
Thunniformes		
Neothunnus macropterus	Yellowfin tuna	Hawaii
Thunnus thynnus	Bluefin tuna	North Sea
Istiophorus americanus	Sailfish	Atlantic

Author	*Sex*	L_∞ (*cm.*)	K	M	T_{max} (*sample*)	L_m (*cm.*)	L_m/L_∞
Clark (1925)	m	17·8	0·33	<1·3	3	11·0	0·62
	f	18·4	0·39		3	11·9	0·65
Hubbs (1921)		9·2	3·7	—	1·3	7·0	0·76
Berdegue (1955)		128	0·3	0·3	15	—	—
Alm (1952)	m	30	0·20	0·29	>16	8–12	≃0·33
	f					13–19	≃0·53
Alm (1952)		34	0·13	0·16	>22	—	—
Radhakrishnan (1957)		37	0·4	—	4	>13	>0·35
Hart (1928) / Ricker (1949)		40	0·14	0·44	13	>32(f)	>0·8
Yokota (1951)	m	105	0·1	1·8(?)	4(?)*	40	0·38
	f	150	0·1	0·4–0·5	7(?)*	44	0·29
Holt (1959*a*)		22	0·7	<2	2	17	0·77
Fitch (1951 and 1956)		40	0·4	0·8–1·0	9	32	0·80
Holt (1959*b*)		46	0·25–0·4	—	4–5	28–33	≃0·67
Appelget & Smith (1951)		119	0·06	<0·8	12	36	0·30
Herald & Rakowicz (1951)		14	2·5	≃1	1	7	0·50
Strawn (1958)		2	12	2–3	1	2	1·0
Moore (1951)		190	0·5	0·8	5	—	—
Tiews (1957)		270	0·6	—	13	—	—
de Sylva (1957)		236	1·1	—	3·5	—	—

protracted than in most higher vertebrates, and as a consequence the maximum size is often not reached within the range of age covered by the data. This makes it necessary to examine in more detail the actual pattern of growth in fish in order to arrive at suitable indices to correlate with longevity.

Fig. 2 gives a few examples of the growth in length of fish. We use length as the measure of body size rather than weight because, as can be seen from Fig. 2, growth in length nearly always follows a simple curve without an inflection.* This is true whether the species is one which can grow to a large or to a small size, and whether it completes its growth pattern rapidly or slowly. Examples of all these are included in Fig. 2.

In the upper part of the diagram is shown the growth of sturgeon (*A. nudiventris*), which both grows slowly (i.e. completes its growth pattern slowly) and also attains a large size, that of sockeye salmon (*O. nerka*; Foerster, 1929) which grows to a fairly large size but does so rapidly, and that of whitefish (*Coregonus clupeaformis*) which grows slowly to a rather smaller size. In the lower part of Fig. 2 are some examples of the smaller species, and for these the scales of both length and age are increased roughly fivefold; to aid comparison, the growth of Lusterfjord herring (*Clupea harengus*; Aasen, 1952) is shown in both parts of the diagram. It will be seen that although the smaller species usually develop their growth pattern more rapidly than do the larger species, there is still quite a range of variation. Thus, for its size, the blenny (*Blennius pholis*; Qasim, 1957) is relatively slow-growing, whereas *Labidesthes* has virtually reached its maximum size in little more than a year; and the 10-spined stickleback (*Pygosteus pungitius*; Jones and Hynes, 1950), although growing to little more than half the size of *Labidesthes*, takes several years to do so.

* Since the growth of most fish is closely isometric after the juvenile phase, the curve of growth in weight is approximated to by cubing that of growth in length. This produces a weight-growth curve which has an inflection at about one-third of the asymptotic weight.

It is found that all the growth curves shown in Fig. 2 and, indeed, those for a great many other species of fish, can be adequately represented by the mono-molecular or inverse exponential equation which, in its simplest form, is

$$l_t = L_\infty (1 - e^{-Kt}) \qquad (1)$$

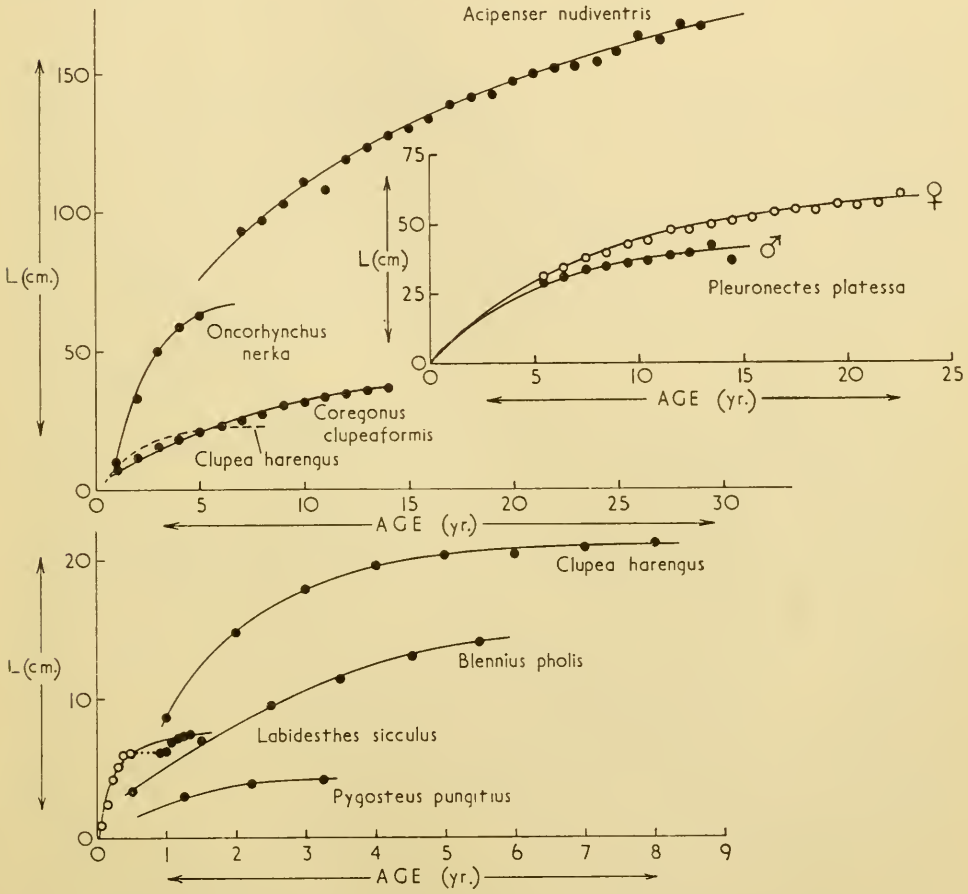


FIG. 2. Some examples of curves of growth in length of fish.

where l_t is the length at age t, L_∞ is the maximum or asymptotic length and K is a constant which determines the curvature of the growth curve, that is, the rate at which the asymptotic length L_∞ is approached (see, e.g. von Bertalanffy, 1938;

Beverton and Holt, 1957). There is evidence that both the constants L_∞ and K have a physiological significance, as will be mentioned later; at this stage we need only regard equation

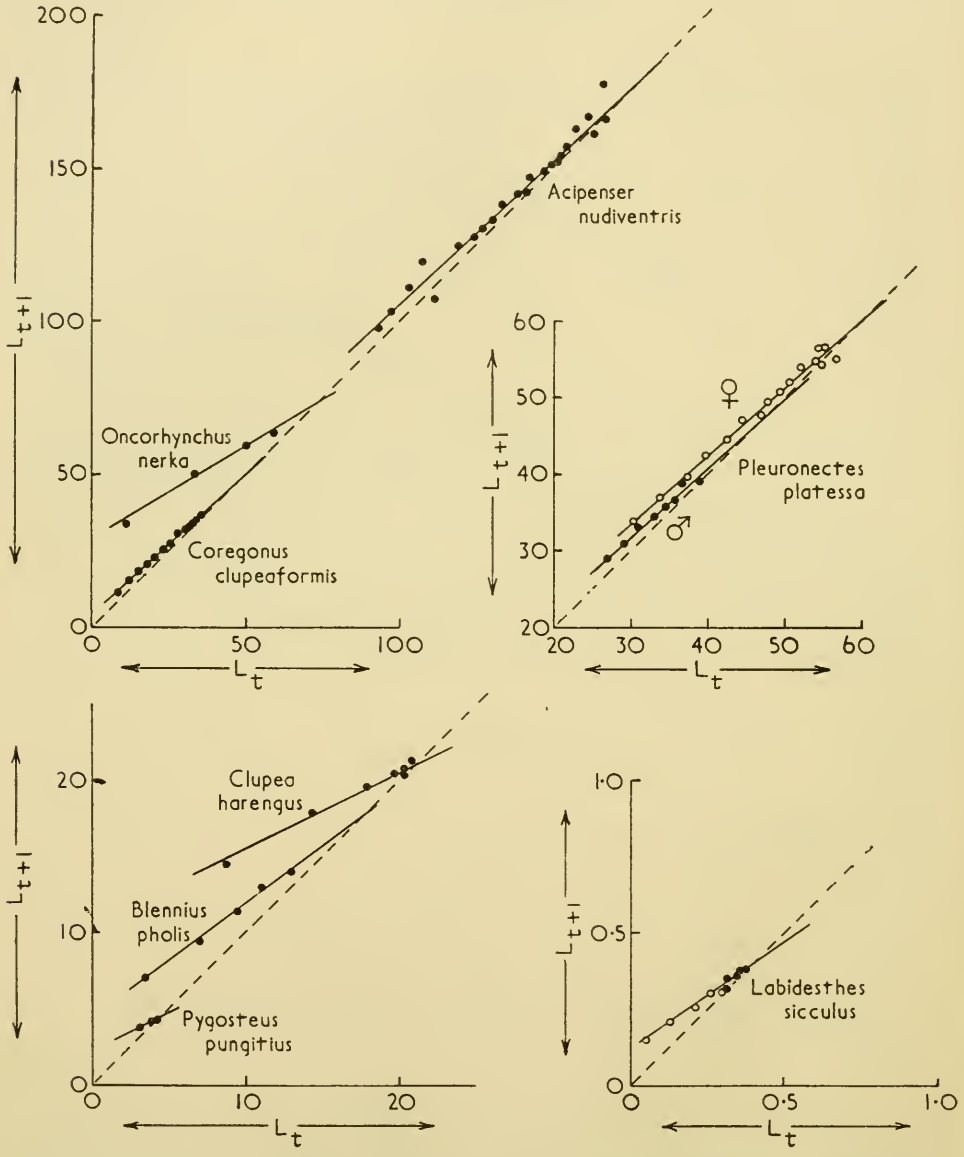


FIG. 3. Growth data of Fig. 2 plotted as length at age t against length at age $t+1$. The slope of the line drawn through the points is e^{-K} and the intersection with the bisector (shown as a broken line) gives an estimate of L.

(1) as a means of representing mathematically the general growth pattern of fish in terms of two parameters to provide a simple means of relating size and growth to mortality and lifespan.

It is a property of equation (1) that it can be transformed to a linear function relating length at age t to length at age $t+1$, namely:

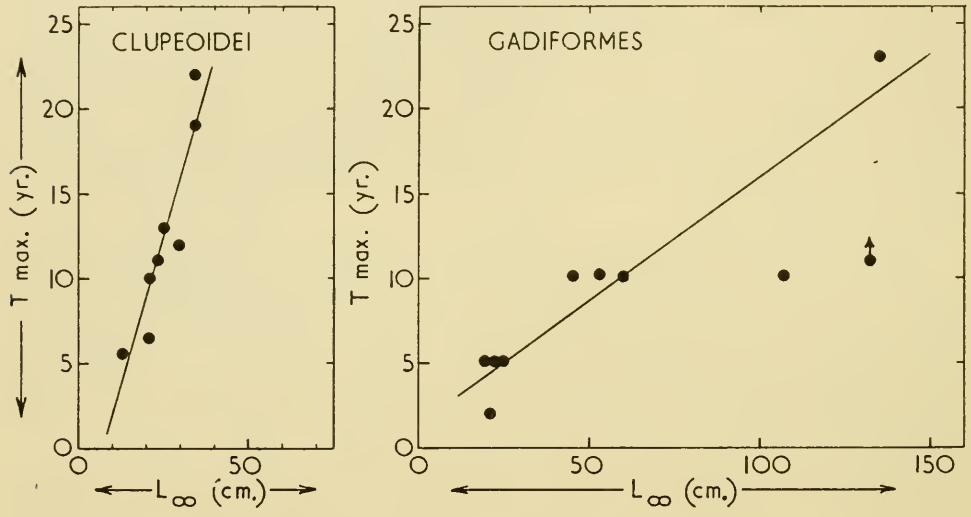
$$l_{t+1} = L_\infty (1 - e^{-K}) + l_t e^{-K} \qquad (2)$$

Fig. 3 shows the growth curves of Fig. 2 plotted in this way. From equation (2) it will be seen that the slope of the line drawn through the points provides an estimate of e^{-K}, and hence of K; and that the intersection of the line with the bisector drawn through the origin (shown by broken lines in Fig. 3) gives an estimate of the asymptotic length L_∞. Estimates of L_∞ and K for all the species under consideration are listed in Table I.

Apart from providing a means of estimating the two parameters of the growth equation (1), plotting l_t against l_{t+1} in this way is a valuable technique for the comparative analysis of growth curves (Walford, 1946). For example, it can be seen from Fig. 3 that male plaice not only have a lower L_∞ than do females, but also grow towards it rather more quickly, i.e. they have a higher K. In the case of *Labidesthes sicculus* (insert in lower part of Fig. 3) the lengths are at monthly instead of yearly intervals, but when plotted one against the next they nevertheless give a close approximation to a straight line; in this case, however, the slope is e^{-12K}, and so in reality is very much flatter than the other graphs of Fig. 3. The method is also useful for detecting departures from the simple growth pattern which sometimes arise because of special environmental conditions, of which lack of uniformity in the supply of food to fish of different sizes is usually the most important (see below and also papers by Alm, 1946, and Deelder, 1951).

Interspecific relations between maximum age (T_{max}), mortality rate (M), asymptotic length (L_∞) and growth rate (K)

Table I lists, for each species, values of a pair of parameters defining lifespan and the force of mortality (T_{max} and M) and a pair defining the asymptotic size of the organism and the rate at which that size is attained (L_∞ and K). The parameters T_{max} and M are, of course, closely linked on purely



mathematical grounds; there is no *a priori* reason why L_∞ and K should be, but it appears from the data that they are fairly closely correlated (inversely), although there are some important exceptions. In this paper we therefore consider only two of the possible relationships, that between T_{max} and L_∞ concerning the extremes of age and size, and that between M and K which, in effect, refer to the course of events within the lifespan. Other possible relationships which might give a better interpretation of the available data are under investigation.

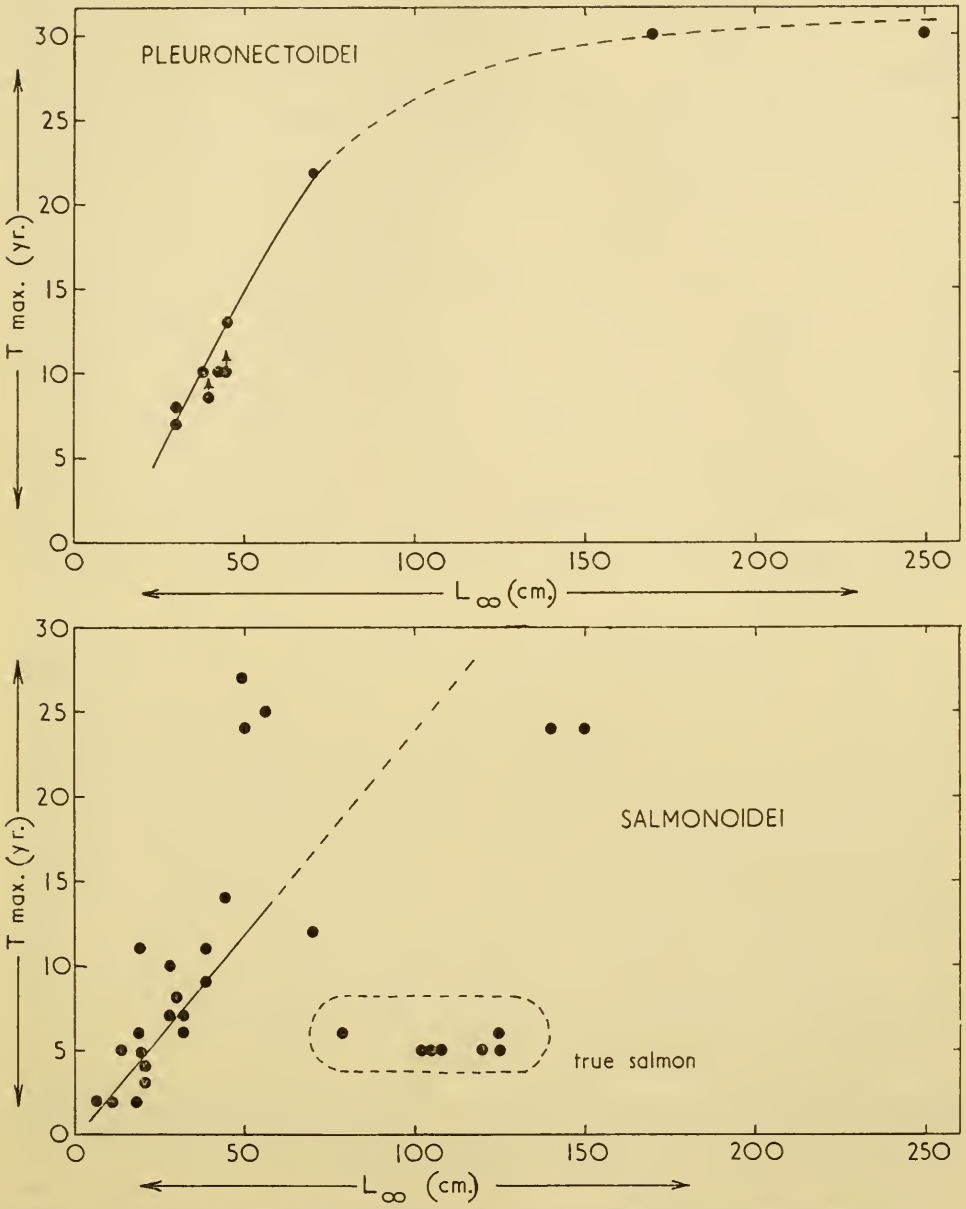


FIG. 4. Relation between maximum age (T_{max}) and asymptotic length (L_∞) in the Clupeoidei, Gadiformes, Pleuronectoidei and Salmonoidei (from Table I). Because the correlation between T_{max} and M, and L_∞ and K, is inverse the species appearing in the bottom left-hand corner of Figs. 4 and 5 tend to occur in the top right-hand corner of Figs. 6 and 7; this point should be borne in mind when comparing the two sets of diagrams.

In four of the main groups of fish there is a sufficient range of values to enable each group to be examined separately. These are the herring and related species (Clupeoidei), the cod family (Gadiformes), the salmonoids (Salmonoidei) and the flatfishes (Pleuronectoidei). Fig. 4 shows the relations between L_∞ and T_{max} in these groups. In each case there is a well-defined trend, especially so in the Clupeoidei which are perhaps a more homogeneous group than the others. The lines drawn through the points have no statistical significance, since the precise accuracy of the individual points is largely unknown, and in some cases the values recorded are certainly over- or under-estimates of the true values; this is particularly so with the parameters T_{max} and M, which are more difficult to determine accurately than are the growth parameters L_∞ and K, and the lines have been drawn with these considerations in mind.

Despite these qualifications, it does seem that the line for the Clupeoidei differs from that for the other groups, the larger members of the herring family appearing to live to a greater age than do fish of the other groups of a comparable size, the contrast being most noticeable with the gadoids. The scatter of the points is most marked in the salmonoids, which may be a reflection of the heterogeneity of this group and of the varied environments in which members of it are found, since they include marine, freshwater and anadromous species. The true salmon, ringed by a broken line, fall outside even the considerable variation of the rest of the salmonoids, since for their size they have a very short lifespan indeed. The pleuronectoids form a compact group, with a closely linear relation between L_∞ and T_{max}, with the exception of the halibut; the maximum age recorded for this species (30 years) may, however, be somewhat below the real maximum owing to difficulties of determining the true age of the oldest fish, and the fact that there was some fishing on the populations in question.

The lines drawn for the four groups shown in Fig. 4 have been reproduced in Fig. 5, together with the data for all other

species. Most of these fall somewhere near the lines for one or other of the first four groups, with the sturgeon in the top right-hand section of the diagram having the highest values of both T_{max} and L_∞, and a cluster of the small and short-lived species near the origin (see enlarged panel). The only

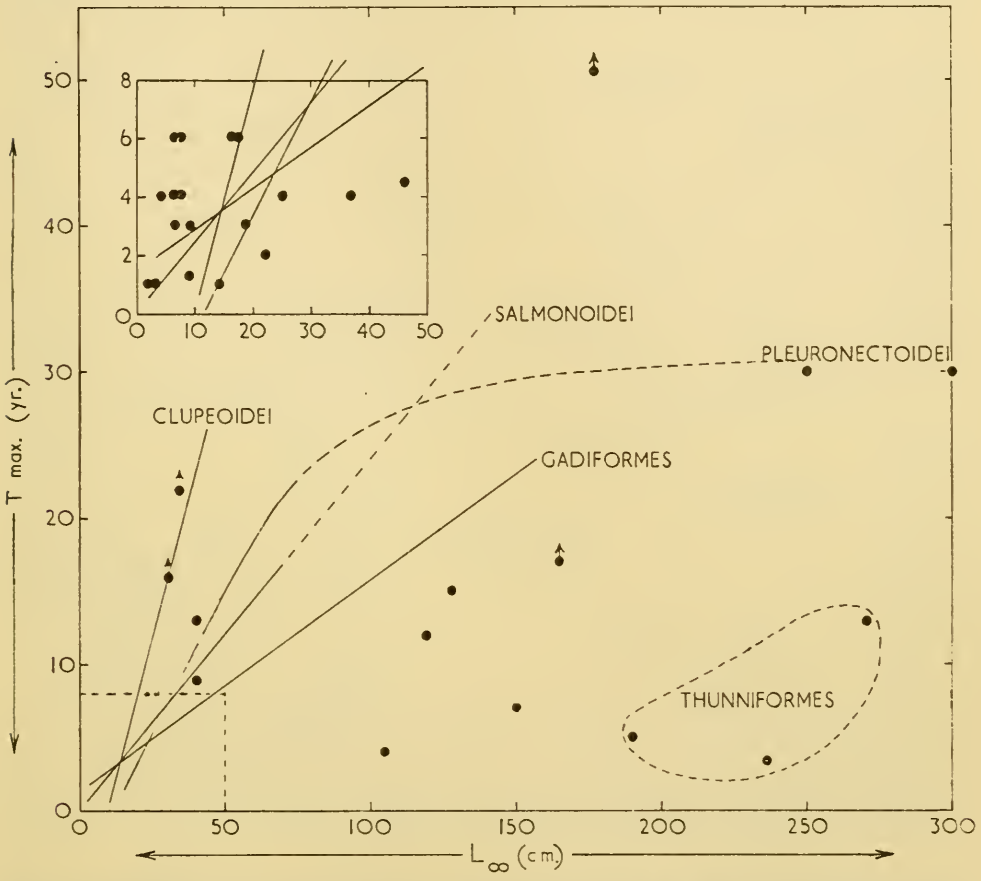


FIG. 5. Relation between maximum age (T_{max}) and asymptotic length (L_∞) in various species not included in Fig. 4 (from Table I). The lines are those for the four groups shown in Fig. 4.

species which, from the data we have examined so far, appear to be exceptional are the Thunniformes—with their large size and relatively short life they occupy a position similar to that of the true salmon—and possibly the Rays (e.g. *Dasyatis akajei*; Yokota, 1951), but age determination is difficult in the

cartilaginous fish and it may well be that the values of T_{max} recorded for this species in Table I are too low (see legend to Table I).

Figs. 6 and 7 show the relations between M and K in the

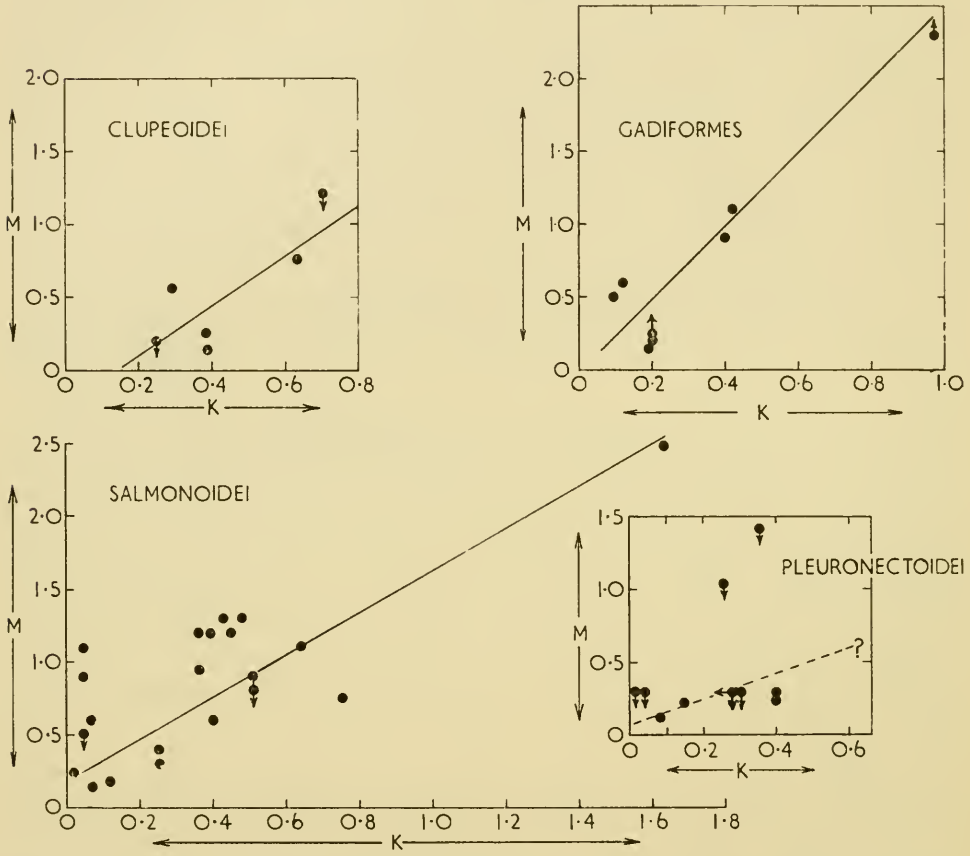


Fig. 6. Relation between natural mortality coefficient (M) and rate of curvature of growth curve (K) in the Clupeoidei, Gadiformes, Pleuronectoidei and Salmonoidei (from Table I).

same way as do Figs. 4 and 5 for T_{max} and L_∞. Again there is a fairly definite trend within most groups, although the scatter is rather greater than before and a trend in the case of the pleuronectoids is hardly detectable. Part, at least, of this greater variation is due to inaccuracies or uncertainties in the

values of M, and in several instances it has been necessary to draw an arrow indicating the direction in which the true value of M is thought to lie. However, when the remaining values are superimposed on those for the four main groups (Fig. 7), a rather more ordered picture is produced than that of Fig. 5. Of the previously aberrant species, the Thunniformes now fall

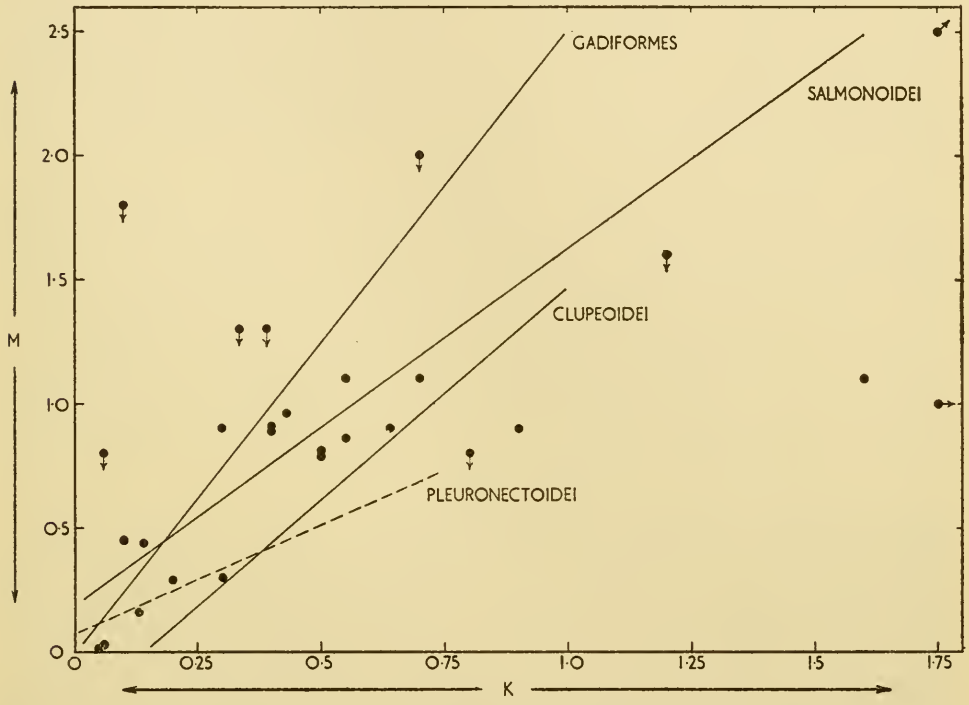


Fig. 7. Relation between natural mortality coefficient (M) and rate of curvature of growth curve (K) in various species not included in Fig. 6 (from Table I). The lines are those for the four groups shown in Fig. 6.

into line, because although they grow to a relatively large size they approach it rapidly, i.e. they have a high K. The same is true for the Atlantic salmon (*Salmo salar*; Nall, 1927) since this also has a relatively high value of K; so indeed have the Pacific salmons (*Oncorhynchus* spp.), although the trend of mortality with age is so abruptly discontinuous in these species that a single value of M cannot be assigned to all of them.

Because both T_{max} and M, and L_∞ and K, are themselves fairly closely correlated (inversely), it is not unexpected that if a relationship is found between T_{max} and L_∞ one should also appear between M and K. What is perhaps significant is that the clearly established exceptions to the general positive correlation between longevity and size (which undoubtedly emerges from the above analysis) are those species which have a much higher value of K than would be expected from their L_∞. This suggests that the "rate of completion of the growth pattern" is more closely related to longevity than is size and some further evidence on this point is discussed below. Be that as it may, we have not yet come across a slow-growing species which dies from natural causes when only a small fraction of its growth pattern has been covered, or the converse—a species whose natural lifespan extends far beyond the point at which the limiting size is reached (as in man); and it seems that for a wide range of fish species the natural span of life is nicely adjusted to the time needed to complete, or nearly to complete, the growth pattern.

Some intra-specific comparisons

We have so far looked at the relations between growth and mortality in different species, but intra-specific comparisons also throw some light on this question. If, firstly, we consider differences between sexes we notice that, when the growth rates are clearly different, L_∞ for males is usually less than for females in the same population (*Dasyatis akajei*, *Gadus minutus*, *Gambusia*, *Cottus*, *Isopsetta*, *Pleuronectes*). In these cases K for males is greater than for females, and the male mortality rate is higher. When the growth rates do not differ, or differ only slightly, the natural mortality rates are also similar (*Leucichthys artedi*, *L. kiyi*, *Salvelinus*, *Mallotus*, *Leuresthes*, *Citharichthys*). The chum salmon (*Oncorhynchus keta*) of the Columbia River is exceptional: the male natural mortality is greater than that of the female, and the male has a higher L_∞. In *Callionymus*, also, the males approach a

greater size; they have a lower K than the females, but a higher mortality rate. In plaice (*Pleuronectes platessa*) of the North Sea, and perhaps in other species, the sexual difference in mortality rates is not simple; thus in both sexes the mortality rate tends to vary with the age of fish, but whereas in males it increases with increasing age—at least from the fifth to about the fourteenth year—in the females the evidence is that it may even decrease. A species of mosquito fish, *Gambusia holbrooki*, gives evidence that males are more susceptible than females to adverse conditions of temperature, oxygen, ion concentration and presence of cyanide. The females also overwinter more successfully and are less severely affected by catastrophies due to unknown causes (Geiser, 1924). It would be interesting to know whether similar sexual differences have been noticed in the many tests which have been made with several fish species of the toxicity of various substances, especially those found in polluted water; we have not, however, found information of this kind in the published reports of such experiments.

Analysis of growth rates within populations of the same or closely related species living in different areas suggests that two factors account for most of the variation found: food and temperature. The asymptotic size is greatly modified by the supply of food available, but this does not affect the parameter K. Differences in environmental temperature, however, affect both K and L_∞; thus with an increase in water temperature K increases roughly proportionally with the logarithm of temperature and L_∞ decreases, but to a lesser extent (see Taylor, 1958; Holt, 1959*a*).

This temperature relation at least partly explains the statement often repeated in fisheries literature that in warmer waters the fish tend to be smaller than in cooler waters but, equally, that they grow faster in the former (see e.g. d'Ancona, 1937; Gunter, 1950); the size distribution that is actually observed at any time depends, however, on the mortality rate as well as the growth pattern. There are rather few data

which can be used to examine this question, but those we have seen suggest that in this case also a high value of K is associated with both a low L_∞ and a high mortality. This can be seen for *Gadus minutus* in Table I, and there is other scattered—but usually incomplete—evidence pointing in the same direction. Thus the grayling (*Thymallus signifer*) has a higher K and lower L_∞ in Michigan lakes (warmer) than in the Great Bear Lake (colder) and it apparently lives about twice as long in the latter locality as in the former (Brown, 1943; Miller, 1946). It is said that in France, where it grows fast, the stickleback (*Gasterosteus aculeatus*) lives only 14–18 months, whereas in northern Europe it lives much longer, and indeed does not mature until it is several years old (Bertin, 1925); according to Flower (1935), sardines (*Sardina pilchardus*) grow more slowly and live longer in the English Channel than in the south of the Bay of Biscay; and so on. Jenkins, Elkin and Finnell (1955) studied the growth of six species of sunfish (*Lepomis* spp. and *Chaenobryttus*) in over one hundred water bodies in Oklahoma and noted for each species that the oldest individuals were always in the populations having the slowest growth rates. We have to be careful in interpreting data of this kind, however, because a general observation that the maximum age attained is lowest in areas where growth is fastest may sometimes be due to effects of fishing coupled with a density-dependent growth rate, the fishing causing a reduced survival and population density and so permitting a better supply of food per fish with a consequent increase in the growth rate (see, for example Fry, 1936, for populations of *Hesperoleucus venustus* in Californian streams).

It is interesting to note that the same associations we have recorded above between growth and longevity in related species, or even in populations of the same species which have become established as independent units in different water basins, do not necessarily hold when growth is modified experimentally. There is not much information on this, but the studies of Alm (1946) on perch populations with stunted

growth did not indicate any marked difference in longevity compared with those in which growth was normal. The experimental studies being carried out by Comfort (personal communication) on growth and longevity in guppies (*Lebistes reticulatus*) appear so far to be giving the same result, although severe underfeeding during the early life of trout kept in tanks has been shown to delay maturity and actually prolong life (McCay, Dilley and Crowell, 1929). Again, the association between high values of M and of K noted above may not hold for comparisons between populations of the same species in closely adjacent waters, as in the case of the bullhead (*Cottus gobio*; Smyly, 1957) in Lake Windermere and the River Brathay (see Table I).

Mortality, growth and metabolic rate

To understand the relations tentatively identified above, it is necessary to extend our studies to include comparative physiology and behaviour, and at this stage we can do little more than indicate the lines of comparison that might profitably be pursued. One of these follows from the fact that the growth parameter K is predictable from the rate of endogenous nitrogen excretion by a starved animal (von Bertalanffy, 1938), and it would be expected that this is also closely related to metabolic rate and to activity, as Edmonds (1957) has shown in a comparative study of some invertebrate groups. For fish, the available data seem to confirm the relation of K to metabolic rate. Thus the oxygen consumption of *Gadus callarias* at 7–11° is 0·33–0·35 O_2 ml./g.$^{2/3}$/hr. and that of *Gadus virens* at the same temperature is similar, 0·36–0·47 O_2 ml./g.$^{2/3}$/hr. (Sundnes, 1957). These two species have the same K values (0·2) though the natural mortality of *G. callarias* is possibly rather higher than that of *G. virens*. On the other hand, *Leucichthys sardinella* has, at about the same temperature (7–9·4°), an oxygen consumption of 0·55–0·75 O_2 ml./g.$^{2/3}$/hr., corresponding with a higher K value (0·4) and much higher M (0·6). The cyprinids *Labeo rohita*,

Catla catla, and *Carassius carassius*, all of which have rather low values of K, have a low oxygen consumption of about 0·2 ml./g.$^{2/3}$/hr. (Blazka, 1958). Over the temperature range 5–35°, oxygen uptake by another cyprinid, the goldfish, *Carassius auratus*, ranges from 0·05–0·46 ml./g.$^{2/3}$/hr. (Fry and Hart, 1948); this species has a K value of about 0·3.

Metabolic rate has been estimated, in connexion with experiments on the transport of live fish in closed containers, from the rate of carbon dioxide accumulation; in one such case *Tilapia mossambica*, which has a higher K value than *Cyprinus carpio*, respired faster than the latter, though kept at the same temperature (Vaas, 1952). Further evidence of relative metabolic rates comes from studies of the rate of uptake and loss of radioactive substances by fishes. Thus, in a review of this subject, Boroughs, Chipman and Rice (1957) quote results indicating that the exponential loss coefficient of orally administered strontium 89 from the body of *Tilapia mossambica* is two and a half times that of skipjack (*Euthynnus yaito*), yellow-fin (*Neothunnus macropterus*) and "dolphin" (*Coryphaena hippurus*). These latter fishes are more active species than *Tilapia* and, from the scanty data available, appear to have higher K values. We have not found any published data to indicate whether, in fish for which K is higher in males than in females, the respiratory rate of males is also higher, as might be expected.

Natural death and reproduction

The last line of evidence we shall mention is that concerning the connexion, in fish, between natural death and reproduction. We have previously mentioned that in the short-lived species where there is an abrupt end to the lifespan, death usually occurs at or soon after spawning. What has been called "reproductive drain" may also become apparent in other ways. For example, the ratio of the weight of a fish to the cube of its length (called the "condition factor" or "ponderal index" in fisheries literature) varies seasonally,

being highest just before spawning. In the plaice it is apparent that this variation is very much greater in older than in younger individuals, and it seems that as the fish gets older (or, perhaps, merely bigger) the strain of meeting the reproductive demand increases to a point at which recovery is not possible. It seems that this kind of effect is most evident in species with high K, which mature at an early age but at a size which is rather large in relation to the asymptotic length, L_∞. Fish, such as sturgeon, with a low K, which mature when relatively rather small, do not show a decline in their reproductive capacities; *Gambusia affinis*, on the other hand, exhibits an absolute decrease in brood size with increasing age (Krumholz, 1948) and indeed this species seems to have a true post-reproductive phase, which is rather rare in fish. Further evidence on the decline in reproductive powers with age in fish is presented in the contribution by Gerking to this colloquium.

The complexity of the relations between the growth and reproduction parameters and mortality rates is illustrated by Svärdson's (1943) review of data for the guppy, *Lebistes reticulatus*. Male guppies mature before females, and die younger. Under experimental conditions of low food supply they grow slowly to a low asymptotic size, and mature late; with a medium food supply the final size is greater and maturity somewhat earlier, but with an abundant food supply the final body size is again lowered although the onset of maturity is still further accelerated.

Other observations concerning the relations between growth, reproduction and death have to be fitted into the picture outlined in this paper, but pending a detailed survey of the known facts, can only briefly be mentioned here. It has been thought for many years that the onset of sexual maturity in fish is a function of their size rather than of their age but like most such generalizations this is only partly true since, within a species population, individuals reach maturity over a considerable range of both age and size. There is, in

fact, a considerable amount of data on the size at which fish first reach maturity, and we have investigated whether the average length at which maturation occurs (L_m) in relation to the asymptotic length (L_∞) has any bearing on longevity. Thus, in the last column of Table I are given the ratios L_m/L_∞, and in Fig. 8 these are plotted against maximum age, T_{max}. The points are very much scattered, although there is perhaps

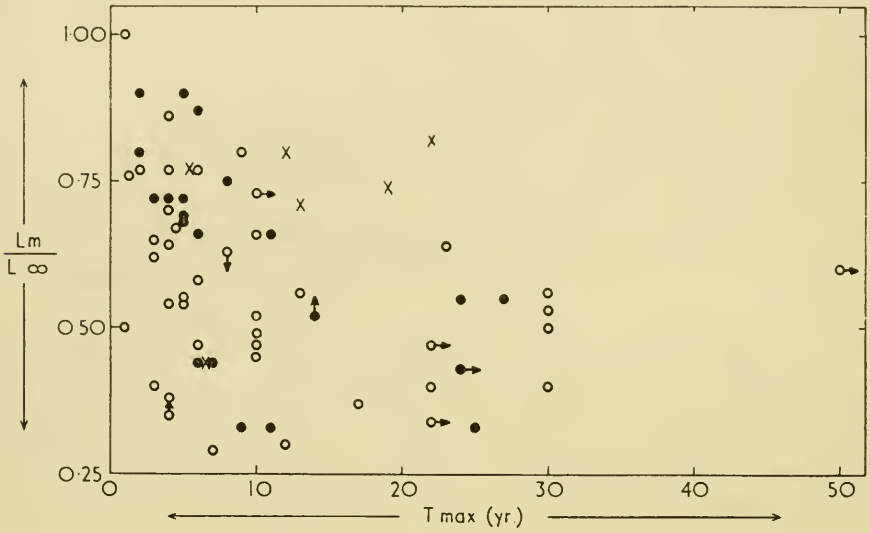


FIG. 8. Size at maturity (L_m) and longevity. Plot of ratio L_m/L_∞ against T_{max}. ● = Salmonoidei, × = Clupeoidei; other species shown as ○.

just a hint that the shortest-lived species are those which have, on average, the highest value of L_m/L_∞, that is, mature at a relatively late stage in their growth cycle. This tendency is a little clearer within the salmonoid group (solid circles), but in the clupeoids (crosses), with one doubtful exception, the values of L_m/L_∞ are consistently high and have no trend at all. It may, of course, be that this way of relating maturity and longevity is too crude; maturation size might better be expressed, for example, as a function of both K and L_∞, but this needs further examination.

The undoubted association between reproduction and death in many species of fish makes it difficult, merely on the kind of evidence we have considered in this paper, to detect whether true senescent processes play a part in determining longevity in fish, as they do, for example, in mammals. The mathematical representation of the characteristic growth pattern in fish which we have adopted here does, of course, imply that growth proceeds towards a finite limiting size, and so is not "indeterminate" in the sense used by Bidder (1932). When the growth of fish is plotted as in Fig. 3 the impression gained is not only that this is a valid interpretation but also that the growth pattern of the long-lived species (including plaice) does not differ qualitatively from that of the short-lived ones in which a limiting size is effectively reached within the observed range of age. As Comfort (1956) has pointed out, however, Bidder's hypothesis of immortality in fish does not necessarily depend on whether there is a finite limit to their growth or not, and can equally well be maintained if that limit can be shown to be approached asymptotically—and hence reached only after an infinite span of time—as opposed to abruptly, with growth ceasing beyond a certain specific age. To test this latter alternative directly, at least in the slow-growing species, is as difficult as it is to prove whether or not there is a finite limit to the lifespan of a species which has a constant mortality rate within the observed range of age. In this connexion, it is perhaps worth noting that although the growth equation we have adopted requires an asymptotic approach to a limiting size, high enough values of K (as are found, for example, for *Labidesthes sicculus*) can produce a theoretical growth curve in which the approach to L_∞ is so rapid that it would be indistinguishable in practice from an abrupt approach, especially when it is remembered that there is usually a seasonal periodicity of growth superimposed on the general pattern.

Thus we are inclined to the view that further speculation along these lines is unlikely to contribute much to the solution

of the question as to whether ageing in fish differs fundamentally from that in higher vertebrates. A more profitable approach would seem to lie in a better understanding of the intrinsic causes of natural death in fish, about which relatively little is yet known. A recent study of the European eel (*Anguilla anguilla*) by Tucker (1959) suggests that the debility of these fish at the inception of gonadal and other hormone activity, which causes them to drift passively downstream, is due to demineralization of the starving body. That this process is reversible, at least in the early stages, is shown by the fact that silver eels imprisoned in fresh water can survive by regression of the gonads and consequent remineralization of the body fluids; and it is also known that recovery of the Atlantic salmon (*Salmo salar*) after spawning can be hastened by placing them in salt water. It is true that both these species, and more especially the eel, have a highly atypical life history, but this kind of explanation of certain behavioural patterns in physiological terms would appear to be an essential step in the solution of at least some aspects of the problem of longevity in fish. The other line of investigation that would seem to be of special significance is a comparative study of the physiology of growth and reproduction in species which have a post-reproductive phase. We would hope that an understanding of the beginning of the reproductive phase of the life history in relation to growth processes would help interpretation of those events at the end of the reproductive lifespan that lead to death.

REFERENCES

Aasen, O. (1952). *Fiskeridir. Skr. Havundersøk.*, **10**, (2).
Akyuz, E. (1959). Unpublished data, filed at FAO, Rome, and Et ve Balik Kurumu, Istanbul.
Alm, G. (1946). *Rep. Inst. Freshw. Res. Drottning.*, **25**.
Alm, G. (1952). *Rep. Inst. Freshw. Res. Drottning.*, **33**, 17.
d'Ancona, U. (1937). *Rapp. Comm. int. Mer Médit.*, **10**, 162.
Anonymous (1954). *Comm. Fish. Rev.*, **16**, 28.
Appelget, J., and Smith, L. L. (1951). *Trans. Amer. Fish. Soc.*, **80**, 119.
Arora, H. L. (1951). *Calif. Fish Game*, **37**, 3.

Berdegue, J. (1955). *Rev. Soc. mex. Hist. nat.*, **16**, 45.
Bertalanffy, L. von (1938). *Human Biol.*, **10**, 181.
Bertin, L. (1925). *Ann. Inst. Oceanogr.*, **2**, 1.
Beverton, R. J. H. Unpublished.
Beverton, R. J. H., and Holt, S. J. (1957). *Fish. Invest., Lond.*, Ser. 2, **19**.
Bidder, G. P. (1932). *Brit. med. J.*, **2**, 583.
Blackburn, M. (1950). *Aust. J. Mar. Freshw. Res.*, **1**, 155.
Blazka, P. (1958). *Physiol. Zoöl.*, **31**, 117.
Boroughs, H., Chipman, W. A., and Rice, T. R. (1957). *U.S. Nat. Acad. Sci./Nat. Res. Counc., Publ.* 551, 80–87.
Brown, C. J. D. (1943). *J. Wildlife Mgmt*, **7**, 353.
Brown, M. E. (Editor). (1957). The Physiology of Fishes. New York: Academic Press.
Burd, A. C. Unpublished.
Chang, Hsiao-Wei. (1951). *J. Mar. biol. Ass. U.K.*, **30**, 281.
Clark, F. N. (1925). *Fish Bull., Sacramento*, No. 10.
Clark, F. N. (1940). *Calif. Fish Game*, **26**, 39.
Cohen, D. M. (1954). *Stanf. ichthyol. Bull.*, **4**, 167.
Comfort, A. (1956). The Biology of Senescence. London: Routledge and Kegan Paul.
Deason, H. J., and Hile, R. (1947). *Trans. Amer. Fish. Soc.*, **74**, 88.
Deelder, C. L. (1951). *Hydrobiologia*, **3**, 357.
de Sylva D. (1957). *Bull. Mar. Sci. Gulf Caribb.*, **7**, 1.
Devold, F. (1938). *Fiskeridir. Skr. Havundersøk*, **5**, (6).
Dickie, L. M., and McCracken, F. D. (1955). *J. Fish. Res. Bd Can.*, **12**, 187.
Dymond, J. R. (1933). *Contr. Canad. Biol.*, **8**, 1.
Edmonds, S. J. (1957). *Aust. J. Mar. Freshw. Res.*, **8**, 131.
Fitch, J. E. (1951). *Fish. Bull., Sacramento*, No. 83.
Fitch, J. E. (1956). *Calif. Fish Game*, **42**, 143.
Flower, S. S. (1935). *Proc. zool. Soc. Lond.*, 265.
Foerster, R. E. (1929). *Contr. Canad. Biol.*, **5**, 1.
Franca, P. da (1953). *Bull. Soc. portug. Sci. nat.*, **4**, 198.
Frost, W. E. (1943). *J. Anim. Ecol.*, **12**, 139.
Frost, W. E. (1945). *J. Anim. Ecol.*, **14**, 106.
Frost, W. E., and Smyly, W. J. P. (1952). *J. Anim. Ecol.*, **21**, 62.
Fry, D. H. (1936). *Calif. Fish Game*, **22**, 64.
Fry, F. E. J., and Hart, J. S. (1948). *Biol. Bull., Wood's Hole*, **94**, 66.
Geiser, S. W. (1924). *Biol. Bull., Wood's Hole*, **47**, 175.
Gerking, S. D. (1959). This volume, p. 181.
Gottlieb, E. (1957). "On the dynamics of the population of coal-fish, *Gadus virens* L., in Norwegian waters." MS.
Grainger, E. H. (1953). *J. Fish. Res. Bd Can.*, **10**, 326.
Gunter, G. (1950). *Copeia*, 298.
Hanyu, I. (1956). *Bull. Jap. Soc. sci. Fish.*, **21**, 991.
Hart, J. L. (1928). *Publ. Ont. Fish. Res. Lab.*, No. 34.

Hart, J. L. (1931). *Contr. Canad. Biol.*, **6**, 427.
Hart, J. L. (1948). *Trans. roy. Soc. Can.*, **42**, (Ser. III), 65.
Herald, E. S., and Rakowicz, M. (1951). *Aquarium J.*, **22**, 234.
Hile, R. (1936). *Bull. U.S. Bur. Fish.*, **48**, 211.
Hile, R., and Deason, H. J. (1934). *Trans. Amer. Fish. Soc.*, **64**, 231.
Holt, S. J. (1959*a*). *J. Cons. int. Explor. Mer*, **24**, 374.
Holt, S. J. (1959*b*). Draft Report of International Training Centre on the Methodology and Techniques of Research on Mackerel (*Rastrelliger*). Rome: FAO, Mimeo.
Hubbs, C. L. (1921). *Ecology*, **2**, 262.
Jenkins, R., Elkin, R., and Finnell, J. (1955). *Oklahoma Fish res. Lab. Rep.*, **49**.
Jones, J. W., and Hynes, H. B. N. (1950). *J. Anim. Ecol.*, **19**, 59.
Kennedy, W. A. (1943). *Publ. Ont. Fish. Res. Lab.* No. 62.
Kennedy, W. A. (1954). *J. Fish. Res. Bd Can.*, **11**, 827.
Krumholz, L. A. (1948). *Ecol. Monogr.*, **18**, 1.
Lea, E. (1930). *Rapp. Cons. Explor. Mer*, **65**, 100.
McCay, C. M., Dilley, W. E., and Crowell, M. F. (1929). *J. Nutr.*, **1**, 233.
Margetts, A. R. Unpublished.
Marr, J. C. (1943). *Stanf. ichthyol. Bull.*, **2**, 157.
Menon, M. D. (1950). *J. Mar. biol. Ass. U.K.*, **29**, 185.
Miller, R. B. (1946). *Copeia*, 227.
Moore, H. L. (1951). *Fish. Bull., U.S.*, **52**, 132.
Nall, G. H. (1927). Fisheries, Scotland, Salmon Fish., II.
Nigrelli, R. F. (1959). This volume, p. 212.
Paccagnella, B. (1948). *Arch. Oceanogr. Limnol., Venezia*, **5**, 141.
Phillips, J. B. (1948). *Fish. Bull., Sacramento*, No. 71, 5.
Probst, R. T., and Cooper, E. L. (1954). *Trans. Amer. Fish. Soc.*, **84**, 207.
Pycha, R. L. (1956). *Calif. Fish. Game*, **42**, 23.
Qasim, S. Z. (1957). *Proc. zool. Soc. Lond.*, **128**, 161.
Radhakrishnan, N. (1957). *Indian J. Fish.*, **4**, 254.
Raitt, D. S. (1939). *Rapp. Cons. Explor. Mer*, **110**, 65.
Ricker, W. E. (1949). *Trans. Amer. Fish. Soc.*, **77**, 114.
Ricker, W. E. (1958). *Bull. Fish. Res. Bd Can.*, **119**.
Robertson, J. A. (1938). *Fish. Invest. Lond.*, Ser. 2, **16**, (2).
Rollefsen, G. (1954). *Rapp. Cons. Explor. Mer*, **136**, 40.
Runnstrom, S. (1936). *Fiskeridir. Skr. Havundersøk.*, **5**, (2).
Sacher, G. (1959). This volume, p. 115.
Sato, R. (1950). *Tohoku J. agric. Res.*, **1**, 87.
Shiraishi, Y. (1957). *Bull. Freshw. Fish. Res. Lab., Tokyo*, **7**, 33.
Silliman, R. P. (1943). *Spec. sci. Rep. U.S. Fish Wildl. Serv.*, No. 24.
Smyly, W. J. P. (1957). *Proc. zool. Soc. Lond.*, **128**, 431.
Strawn, K. (1958). *Copeia*, 16.
Sundnes, G. (1957). *Fiskeridir. Skr. Havundersøk.*, **11** (9).
Svärdson, G. (1943). *Rep. Inst. Freshw. Res. Drottning.*, **21**.

TAYLOR, C. C. (1958). *J. Cons. int. Explor. Mer*, **23**, 366.
TEMPLEMAN, W. (1948). *Bull. Newf. Govn. Lab.*, **17**.
TESTER, A. L. (1937). *J. biol. Bd Can.*, **3**, 108.
THOMPSON, W. F., and BELL, F. H. (1934). *Rep. int. Fish. Comm.*, **8**.
THOMPSON, W. F., and HERRINGTON, W. C. (1930). *Rep. int. Fish. Comm.*, **2**.
TIBBO, S. N. (1957). *Bull. Fish. Res. Bd Can.*, **111**, 85.
TIEWS, K. (1957). *Ber. Dtsch. Komm. Meeresforsch.*, **14**, 192.
TUCKER, D. W. (1959). *Nature (Lond.)*, **183**, 495.
VAAS, K. F. (1952). *Proc. Indo-Pacif. Fish. Coun.*, **3**, 119.
VIVES, F., and SUAU, P. (1956). *Invest. Pesq.*, **5**, 17.
VNIRO (1949). Ministry of Industrial Fisheries. Moscow.
WALFORD, L. A. (1946). *Biol. Bull., Wood's Hole*, **90**, 141.
WOHLSCHLAG, D. E. (1954*a*). *Ecology*, **35**, 388.
WOHLSCHLAG, D. E. (1954*b*). *Stanf. ichthyol. Bull.*, **4**, 189.
YOKOTA, T. (1951). *Bull. Jap. Soc. sci. Fish.*, **16**, 188.

DISCUSSION

Rotblat: Have you also plotted $1/K$ against T_{max}? $1/K$ has the dimensions of time and is proportional to the time it takes to grow to half size. This may also be a linear function of the span of life.

Beverton: No, we have not yet done that; so far we have examined only the relationships between K and M and between L_∞ and T_{max}.

Rotblat: The combination of these two factors is of special interest because you relate, then, time to time. This also agrees with what Sacher said about low metabolic rate.

Beverton: In fish the natural mortality coefficient and the maximum age are closely correlated, because most of the logarithmic survival curves tend to be rather straight. We do not have curves of nearly the same slope which suddenly dip to very different maximum ages.

Danielli: These growth-rate limitations may be entirely due to differences in natural conditions. Have you any data from fish which have been exposed to toxic substances in the water ?

Beverton: The only paper on exposure of fish to toxic substances that I can recall offhand is on *Gambusia* (Geiser, S. W. (1924). *Biol. Bull.* (*Wood's Hole*), **47**, 175). There the investigation was to show that males not only died off more quickly than the females after reproduction but were also more susceptible to a range of toxic substances. In other words, their balance with the environment seemed more precarious than that of the females, with respect to artificially induced hazards as well as natural ones such as reproduction. On the first point, growth is undoubtedly very flexible in fish. Nevertheless,

our impression is that looking over the whole range of growth data for fish it is possible to see fairly characteristic sorts of growth. However much food you give a small fish it never grows very much bigger than its characteristic size in nature. This is a pretty general statement, but despite the extent to which growth can be varied experimentally, there does seem to be an overall pattern in nature which is fairly consistent.

Holt: This sexual difference in susceptibilities is found rather commonly in experiments on the effects of water pollution and in studies to improve the transport of live fish in closed containers; the males are usually more sensitive. Unfortunately I have no good data with which to compare respiration rates of the sexes. Spawning plays a more important part as a factor associated with death in fish, than, for example, food supply. One can vary the growth rate tremendously by adjusting the food supply, without changing the mortality rate at all. But where death is caused through spawning or is associated with it and maturity, it seems that the males are more drastically affected than the females. Thus in one salmon species all the males and most of the females die after spawning, but some of the females return to the sea.

Nigrelli: In aquarium management we constantly find, when we autopsy fish, that there are about three females to one male, which means that there is some sort of selection in the collection.

Danielli: If the fish are dying as a result of spawning perhaps one can change the situation. Death following spawning in salmon is said to be due to some syndrome involving the pituitary. This, surely, could be modified by appropriate hormone treatment.

Nigrelli: Are there any comparative figures on population or growth studies on salmon or trout in hatcheries and those under natural conditions ?

Holt: I do not know.

Nigrelli: I think that in large hatcheries there is a lower infant mortality rate than is found under natural conditions.

Comfort: In these natural populations, is there always a tendency for the growth to be smooth in outline ? Or does the same effect occur in wild fish as I have produced by keeping them small artificially and then increasing the food supply ?

Beverton: Yes; perch is the most notable example. You get that in the wild, particularly where there is a marked change in feeding habits as the fish grow bigger. For example, perch up to about 15 cm. feed primarily on animal plankton such as freshwater shrimps, etc. Above that size they change to exclusively carnivorous habits. If the pond or lake has no supply of small fish they just stop growing.

But the data also show that this stunted growth does not seem to be associated with any marked increase in mortality rate.

Comfort: I think that is what I am going to find.

Another point is that H. J. Van Cleave (1934; 1935. *Ecology*, **15**, 17; **16**, 101) suggested that the apparent senescence of some molluscan species which are more or less indeterminate in growth is actually a size effect, because there is no accumulation of animals in the older age groups. In one of the freshwater limpets the question arose whether, when they got beyond a certain size, their holding-on mechanisms became inefficient or whether they were taken selectively by predators (Hunter, W. R. (1953). *Proc. zool. Soc. Lond.*, **123**, 623). Have you any instance of an adverse size effect in fish ?

Beverton: I should have thought it usually worked the other way in fish. For instance, they escape predation as they get bigger, rather than the reverse, I would say.

Comfort: What about catching them ?

Beverton: That depends on the gear. Usually fishermen are after the bigger fish and take steps to catch them, but not always.

Holt: It is usually in the smaller fish, having rather high K values, that the effect of reproduction on lifespan seems to be greatest, as they die off quickly after reproduction. In fish like sturgeons which grow to large sizes rather slowly there is no noticeable effect of reproduction on their mortality, even though they mature at a relatively small size. In middle-sized fish, such as the plaice, there is a certain effect but not such a drastic one. Thus in large spawning plaice there is a relatively great seasonal variation in the relation of length to weight (what we call the "condition factor"), suggesting that attainment of spawning condition becomes an increasing strain on the fish as they grow older.

Rockstein: Do land-locked salmon reproduce year after year ?

Holt: Some land-locked populations do.

Beverton: There are the "residual" and the "Ko Kanee" salmon (*Oncorhynchus nerka*). Both are non-migratory, but whereas the "residuals" are the progeny of anadromous parents, the "Ko Kanee" is a self-maintaining stock which has no connexion with either of the other two.

Gerking: There are some land-locked Atlantic salmon that reproduce year after year.

Rockstein: In a large reservoir in New York State we have brown trout, also called salmon trout, and these can be caught in all sizes depending on how successful the first year stock is in eluding the angler. It appears from their annual movements into the lake in spring and out again in the fall that they are spawning each year,

something like the salmon. If they do spawn each year, however, then spawning may have no appreciable effect on their longevity, as it is said to have in the case of the salmon.

Gerking: There has been a very good study on those lines in Scotland, but it does not concern the question of ageing. It is a migration pattern.

PHYSIOLOGICAL CHANGES ACCOMPANYING AGEING IN FISHES*

Shelby D. Gerking
Department of Zoology, Indiana University, Bloomington, Indiana

This paper is a review of efforts that have been made to show the relation between age and two important life functions of fishes, nutrition and reproduction. Only a few studies have been made on the effects of age on food conversion, but feeding experiments demonstrate clearly that the ability to convert protein to body flesh declines as size and age increase. Other vertebrates also conform to this pattern, although they achieve a specific size relatively early in life in contrast to the prolonged period of growth in fishes. The rate of decline in the ability to utilize food for growth seems to be a matter of degree, rather than a basic difference between animals of specific and non-specific size.

Studies of the effect of age on reproduction in fishes have produced no general conclusions. Nevertheless, the subject deserves attention because changes in reproductive capacity with age are commonly used as a criterion of senescence in other vertebrates. The reproductive capacity of live-bearing fishes of the family Poeciliidae declines with age and there may be a period of sterility before death. Neither of these two facts apply unequivocally to egg-laying fishes, however. There is no period of reproductive senility, and it is an open question whether or not age has an effect on reproductive capacity. Individual variation in fecundity is so great that age effects cannot be detected by refined statistical techniques. A more

* Contribution No. 668 from the Department of Zoology, Indiana University, Bloomington, Indiana.

subtle change in the ovary has been discovered that has not been appreciated before, however. Egg number does not increase in proportion to ovary weight. Either eggs become larger and fewer or the relative amount of connective tissue increases as the ovary grows. No critical evidence is available to support either contention. If the latter is true, ageing changes in the gonads of fishes would be similar to those in higher vertebrates. The lack of conclusive proof of the effect of age on reproduction is disturbing because it has not been possible to accept or refute without question that portion of Bidder's argument (1925*a*) that fish are immortal because old individuals show no decline in reproductive capacity.

Knowledge about fishes has not progressed to the point where the relative importance of the influence of rate of growth and chronological age on physiological function can be distinguished. This constitutes a great weakness in the analysis of differences in nutrition and reproduction related to size and age. Svärdson (1951) has expressed the opinion that age of fishes should be expressed as "physiological age" based on nutrition and rate of growth. Larkin, Terpenning and Parker (1957) have demonstrated that growth of rainbow trout (*Salmo gairdneri*) in different British Columbia lakes can be dealt with more effectively by comparing growth rates of fish of the same size rather than of the same age. This point of view reflects a tendency to depart from traditional age and growth studies because of dissatisfaction with chronological age as an adequate unit on which to base physiological change. Critical experiments are clearly needed to separate the effects of rate of growth from those of chronological age. In view of the lack of information it has been necessary to refer in the ensuing discussion to age and size indiscriminately without distinguishing which of the two factors is the more important.

Efficiency of Protein Utilization for Growth

A series of studies on the protein metabolism of sunfish, family Centrarchidae, has been done in order to learn whether

or not size and age have an effect on the ability to convert protein to body flesh (Gerking, 1952, 1954, 1955*a*, *b*). Longear sunfish (*Lepomis megalotis*), green sunfish (*Lepomis cyanellus*), and bluegill (*Lepomis macrochirus*) gave similar results. The methods used in these experiments were essentially the same as those used to study food conversion in other animals (Maynard, 1951). A weighed quantity of food was fed each day to a group of fish of various sizes kept in separate aquaria at temperatures of about 25° for a period of 30 to 50 days. They were fed at maximum or near-maximum rates. At the end of the period the fish were killed, weighed, and analysed for protein. At the beginning of the period their weight was known, and their protein composition was estimated by averaging protein determinations by a micro-Kjeldahl method on several fish collected at the same time and place as the ones used in the experiments. The food was mealworms, *Tenebrio molitor* larvae, which had also been analysed for their protein content. Thus the efficiency of protein utilization for growth could be determined for fish of various sizes by comparing the amount retained with the amount absorbed by the gut. Absorption of protein was measured by subtracting the amount of nitrogen in the faeces from that consumed. Absorption was practically complete in every fish.

Menzel (1957) has duplicated these experiments on two Bermuda reef fishes, angelfish (*Holocanthus bermudensis*) and red hind (*Epinephalus guttatus*). The former species is a herbivore and the latter a carnivore. They were fed as much as they would eat at three temperatures, 19, 23, and 28°. The angelfish were fed algae (*Enteromorpha salina* and *Monostroma oxysperma*) which were kept in the tanks with them, and the red hinds were fed three species of small fish, *Harengula callolepis*, *Sardinella anchovia*, and *Anchoa choerostoma*. Efficiency of protein utilization for growth was determined over a 21-day period in the manner described above.

The weight of Menzel's fish varied from 50 to 763 g. and the sunfish from 7 to 184 g. Protein accumulation was used as an

index of the efficiency of the growth process because protein synthesis is the most characteristic feature of growth in animals. The fat content of fishes varies considerably from one individual to another and during the seasons of the year. Such large variations in fat complicate precise growth measurements based on body weight, dry weight, or caloric content.

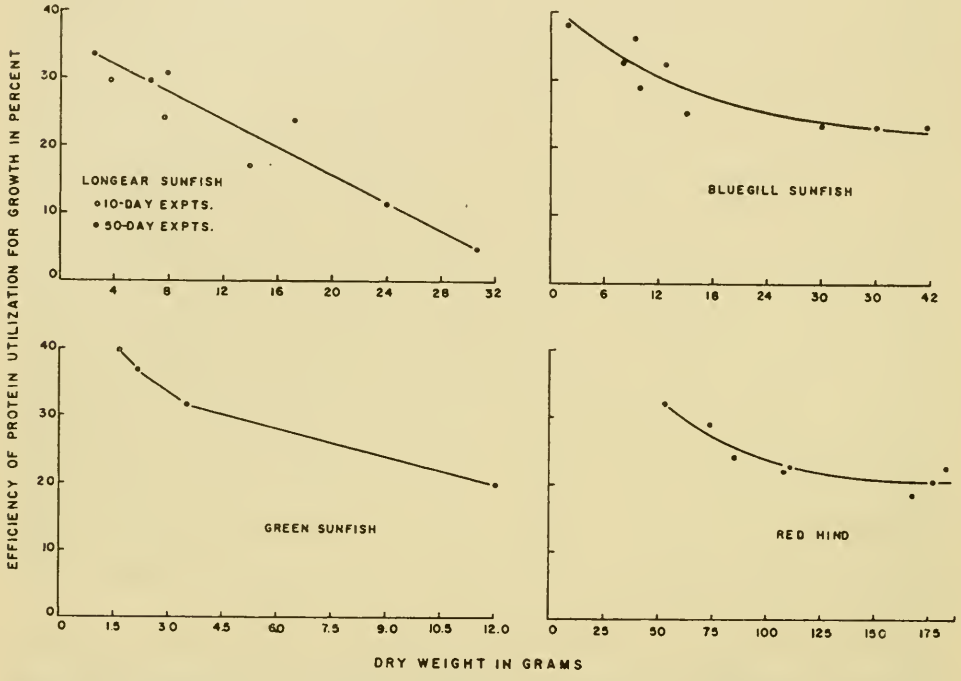


FIG. 1. Relationship between efficiency of protein utilization and dry weight of four species of fish. Sources of information given in text.

With the exception of the angelfish, the other four species fit a common pattern. The efficiency of protein utilization for growth decreases as the fish increase in size (Fig. 1), indicating that either size, age, or both affect the ability of the fish to utilize their food for the synthesis of new protoplasm. The angelfish is a special case because of its herbivorous feeding habits. They were unable to grow on a diet of algae and generally had a negative nitrogen balance. Menzel concluded that angelfish cannot grow on a diet of plants alone unless they

eat extraordinary quantities or algae with a much higher protein content than he used. Probably the "herbivorous" fish depends to a large extent on the invertebrates living in association with plants for the protein required for growth. The results of the experiments on angelfish are, therefore, not comparable with the others.

The experimental results on the four carnivorous species are similar. In every case the efficiency of protein utilization decreased as the size of the fish increased. Efficiency was very high in the smallest fishes. For example, green sunfish (body weight = 7·1 g.) were 39·7 per cent efficient in using protein for growth; longear sunfish (9·1 g.) were 33·3 per cent efficient; bluegills (7·7 g.) 38·0 per cent; and the red hind (about 227 g.) 32·1 per cent. In contrast, utilization among the largest specimens was 20·0 per cent (48·5 g.), 4·7 per cent (103·3 g.), 23·6 per cent (184·0 g.), and 22·7 per cent (612 g.), respectively, for the four species. The value for the largest longear sunfish departs considerably from the others. This specimen was as large as any ever observed in the creek where it was captured near Bloomington, Indiana, and it was probably over six years old. The other three species are not represented by individuals of maximum size or age. This may indicate that extremely large individuals have a very low efficiency of protein utilization for growth. More evidence is required to establish this point, however.

The shape of the graphs is not consistent. A linear relationship expresses the relation between protein efficiency and dry weight in the longear sunfish, but it is curvilinear in the other species. The inconsistency is due to individual variation and the difficulty in establishing the initial protein content of the experimental fish from analyses of sample fish.

Menzel answered an important question with respect to the effect of temperature on protein utilization. The red hind ate only slightly more at 23° than at 19° but ate about twice as much at 28°. This great difference in feeding rate did not alter the efficiencies of protein utilization, however. Thus all

protein utilization experiments in this 9° temperature range are comparable.

A large amount of work has been done on food conversion by fishes, but most of it relates weight gain to the amount of food consumed. Large variations have been encountered and are due to variable fat deposition, unknown organic composition of the food, differences in the size of experimental fish, and other factors. Most of the research has been done on a variety of foods fed to young trout in order to obtain maximum growth rates in hatcheries. This material is not applicable to the present discussion since the fish used in the experiments were nearly uniform in size and age. Ivlev (1939*a*, *b*, *c*), Karzinkin (1939) and Morgulis (1919) have studied fish nutrition by detailed analyses of the organic constituents of the fish and their food, but none of these workers compared the efficiency of food utilization by fish of different sizes.

Although the effect of age and size on protein utilization for growth cannot be separated, it can be stated definitely that larger fish are less efficient in this respect than smaller ones. Chronological age may play some part in this phenomenon. It is universally true that the rate of growth declines as age and size increase. In this respect fishes conform to the common vertebrate pattern. The protein metabolism studies demonstrate that this decline is due to a decreasing ability of the fish to utilize its food for growth as it grows larger and older. The growth of most vertebrates stops relatively early in life while that of fishes is prolonged. Although this difference cannot be explained at the present time, the loss of growth efficiency with age is clearly exhibited by both.

Fecundity

Live-bearing fishes

There are several groups of fish which give birth to well-developed young, but reproduction in relation to age has been studied in only one family, the Poeciliidae. In this family the

male is much smaller than the female. His growth stops soon after sexual maturity is reached, but the female continues to grow until death. Fertilization is internal and the sperm transfer is accomplished by a greatly modified anal fin, the gonopodium, which acts as the male copulatory organ. The sperm penetrate the ovarian wall and fertilize the eggs while they are within the ovarian follicle. Development proceeds, and the young are born in various stages of development according to the species.

Reproduction and senescence have been studied only in the western mosquitofish, *Gambusia a. affinis*. Krumholz (1948) has provided an unusually good series of observations on the number of young in successive broods of females from the onset of sexual maturity until death. Females were collected from ponds in southern Michigan and in the vicinity of Chicago during the summers of 1939 to 1944, and the number of embryos in the ovary was counted. The number of young produced by a single female depends on: (1) the number of broods liberated during a season, (2) the length of the mother fish, (3) the time of season at which the individual broods are cast, and (4) the locality in which the mother fish lives. The first two factors are pertinent to the present discussion.

The age and size at first maturity are correlated with the time of year when the female offspring are born and their rate of growth. Faster-growing individuals generally reach maturity at an earlier date than slower-growing individuals. Mosquitofish born late in the summer do not reach maturity until the following spring while those born early in the summer may reproduce within a month or two. The number of young in a brood increases as the length of the female increases, but at large sizes the rate of increase is drastically reduced. The rate of increase in fecundity in relation to length of the female is greater in the second brood than in the first or subsequent ones. In one case the number of embryos in the first brood increased as the $1 \cdot 3$ power of the length; the second brood as the $1 \cdot 4$ power, and the third brood as the $0 \cdot 8$ power.

Numbers of embryos in the fourth brood were so variable that no relationship with length of the female could be demonstrated.

The influence of age on fecundity was proved by both field and laboratory observations. Females of similar size collected at an earlier date in the summer contained a greater

Table I

THE EFFECT OF AGE ON FECUNDITY OF FEMALE MOSQUITOFISH (*Gambusia affinis*) OF THE SAME SIZE. MODIFIED FROM KRUMHOLZ (1948)

Size of female in mm.	*Date of collection*	*No. of females*	*Average no. of embryos*
		Argonne Woods Pond	
46–55	June 9	63	210·4
	July 13	194	152·9
38–44	July 13	179	153·3
	Aug. 14	3	42·7
		Sanitary—District Lake	
35–44	June 9	67	30·7
	July 13	236	28·4
50–55	July 13	228	28·8
	Aug. 14	449	8·8
		Parr's Lake	
27–45	July 31	330	47·4
	Aug. 14	324	34·3
35–46	Aug. 14	167	49·9
	Sept. 19	25	17·0

number of embryos than those collected later (Table I). The decrease in embryo production was greatest during late summer, near the end of life. Among fish born at approximately the same time there was a decrease in fecundity with age despite an increase in size. One group of females averaged 49 mm. in length and yielded a mean of 205·4 embryos on June 9, 1939; on July 13 the females were 52·6 mm. long and gave 155·7 embryos; and a few remaining fish of the same age

group measured 52·3 mm. on August 14 and contained 42·7 embryos. Under laboratory conditions four fish gave birth to a decreasing number of young. They averaged 30·8 young in the first two broods, 10·0 in the third, and 7·0 in the fourth.

There may be a period of reproductive sterility in *Gambusia* late in life. In one collection the largest female was not gravid while other sexually mature individuals were. The ovaries of this female were examined microscopically, but no ova were found.

The only other pertinent observation in this connexion was made by Fraser and Renton (1940) on *Heterandria formosa*, the dwarf top-minnow. Successive broods were followed in a single female from April 1934 until death in May 1936. She grew to a remarkably large size (40 mm.), and produced a total of 170 young, 150 of which were born during the first eight months. She showed diminishing fertility during the last few months of life. At the time of death the ovary was examined microscopically and found to be a "mass of degenerating tissue".

Egg-laying fishes

Bidder (1925*a*, 1925*b*, and 1932) raised an extremely provocative question when he proposed that fish and certain other aquatic animals are potentially immortal. He based his argument on reproduction and growth in the plaice (*Pleuronectes platessa*). He noted that these fish continue to grow throughout their lives and that the oldest individuals retain their reproductive capacity. His idea was immediately challenged by Wallace (1925) who pointed out that male plaice had a higher mortality rate than females and that "this apparently implies natural death". Bidder answered by making a distinction between "senile death" and "parental death". Parental death refers to that which occurs as a result of the reproductive act. He supported this definition by drawing upon the same plaice data which Wallace had used to show that six-sevenths of the males die after the first spawning

Senile death in Bidder's opinion should be reserved for those animals which exhibit "negative growth" after full sexual maturity and specific growth have been achieved. In his last paper Bidder took his stand on the basis of correlating ageing with specific growth and ceased to make an issue of reproductive performance.

The issue of reproduction was soon raised again by Orton (1929) in a somewhat different manner. He asked the question whether or not fishes might die as a direct or indirect result of expending themselves in reproduction. Russell's (1914) data were cited, which suggested that the reproductive organs of large haddock (*Melanogrammus aeglefinus*) make up a larger proportion of the body weight than they do in smaller specimens. Metabolism is concentrated overwhelmingly on reproduction, and although the expenditure of energy may not kill, the animal may become so unstable that otherwise sublethal factors might be brought into play and cause death. Orton dramatized this effect by terming it "over-reproduction".

Orton's viewpoint turns up in another connexion. Svärdson (1949) considered the effect of natural selection on the egg number of fishes and concluded that there must be opposing selection pressures for decrease as well as an increase in egg number. Clearly, a mutation causing an increase in egg number would have a selective advantage and spread through a population unless there were factors opposing such a change. In his words: "There would be an anatomical and physiological limit for the females' capacity of producing more eggs. When the egg number has been brought up to this limit, only those individuals not exceeding the limit could spawn, while the others died." Svärdson later rejects this as a major factor in evolution and concludes that egg number would be limited by the ability of fish to protect the young among those fishes which behave in this way. More importantly, he thinks, egg number is limited by the premium on large eggs which produce large fry. He postulates that the large fry are in a better competitive position in the population.

Bidder's theory that fish are potentially immortal has never attracted much attention among fishery workers. No doubt its lack of popularity is due to the fact that those who work with fish know that they die and that the lifespan of most species is short compared with our own. Among the host of workers who have aged fish by inspecting the growth rings on the scales or other hard parts, none has observed a specimen which spanned the centuries. Direct observation by aquarium curators throughout the world has led to the same conclusion (S. Hinton, unpublished). Only 21 of 328 species reported lived longer than 20 years. The oldest fish was a sturgeon (*Acipenser ruthenus*) in the Royal Zoological Society Aquarium in Amsterdam, Holland, which lived for 69 years and 8 months. The cause of death was not reported for any species in the list.

On the other hand, Orton's views have led to some hard thinking. There have been several attempts to learn whether or not fishes "over-reproduce" to the point where the effort interferes with other life functions. As we shall see, some studies affirm while others negate this point of view.

Variability. There is a tremendous variation in fecundity, not only in different species but within the same species from place to place and among individuals of the same size. This variation immeasurably complicates studies on the effect of age on fecundity, and as a result the critical studies are of a statistical nature. The following sources of variation should be kept in mind while reviewing the evidence.

1. Size variation. Fecundity increases as the length and weight of the fish increases.

2. Individual variation. Every fecundity study has demonstrated a great individual variation in fecundity for fish of the same length and of the same weight.

3. Geographical variation. The fecundity of individuals of comparable size varies considerably from one locality to another. Määr's (1949) work on the char (*Salmo alpinus*) of the Faxälven Water System, Sweden, has shown that the egg

number per female may vary as much as fivefold in different lakes of the same watershed. In fact, geographical variation has been so prominent that "races" of some species have been delineated partly on the basis of fecundity. Davis (1957) has shown that the ova production of the American shad (*Alosa sapidissima*) varies considerably from one river system of the Atlantic Coast drainage to another, and McGregor (1923) could distinguish certain river races of the king salmon (*Oncorhynchus tshawytscha*) on the Pacific Coast on the basis of egg counts.

4. Year-to-year variations in the same locality. Individuals of the same size may bear significantly different numbers of eggs from one year to the next. This is true for the long rough dab (*Hippoglossoides platessoides*) off the coast of Scotland (Bagenal, 1957*b*) and for the lake trout (*Salvelinus namaycush*) of Lake Opeongo, Ontario, Canada (Fry, 1949).

These wide variations in fecundity are usually explained on the basis of genetic and dietary differences. The racial studies imply that heredity is very important in determining fecundity. Year-to-year variation has been attributed to differences in the availability of food. Both sources undoubtedly account for the fluctuations in the egg number of individuals of the same size.

Because of the complex nature of the information on fecundity, evidence of the ageing process from a few species in which fecundity has received considerable study will be reviewed here.

Methods of counting eggs. The usual methods of determining fecundity vary from counting the entire number of eggs from both ovaries to counting samples from various sections of one or both ovaries and computing the total number of eggs on the basis of the sample. Three sampling methods have been used: volumetric, dry weight, and wet weight. In the first method the total volume of eggs is determined in a graduated cylinder and the number in a

known sample volume is counted. The fecundity is determined by direct proportion. The dry-weight and wet-weight methods are essentially the same except that the counts are made either on eggs which have been dried to constant weight or on eggs taken directly from the preserving fluid.

Like those of other animals, the ovaries of fishes contain eggs in various stages of development. Early workers debated the issue as to which eggs would be spawned. By measuring the diameter of the ova in fish just ready to spawn, by describing their external appearance, and by examining histological sections of the ovary, various categories of eggs were established. A comparison of these observations with those on the ovaries of spent fish was the basis for deciding which eggs to count for an estimate of the fecundity of an individual. These observations have been made in great detail, and they have resulted in learning that not all ripe eggs are shed during the spawning season. Usually the numbers retained are insignificant compared to those that are liberated. Ripe ova which are retained in the ovary quickly degenerate and are resorbed. Such observations have also been responsible for discovering that some species, like the long rough dab, do not spawn every year (Bagenal, 1957*a*) while in others, like the yellowfin tuna (*Neothunnus macropterus*), several batches of eggs may mature during a single, long spawning season (June, 1953).

Herring. Wynne-Edwards (1929) immediately set about testing Orton's hypothesis about a possible disproportionate growth of the gonad in relation to body weight in the herring (*Clupea harengus*). Both ovary and testes reach maximum weight during the spawning season and decrease to an insignificant size immediately after the sexual products have been shed. The cycle of gonad growth then begins again in preparation for the next spawning. Since the reproductive tissue makes up about 20 per cent of the weight of the body at maturity, a considerable amount of the anabolic process is concentrated on the maturation of the sex organs.

Wynne-Edwards argued that if the gonads of mature fish increase in weight each year at a rate greater than that of the body, then the increasing tax of spawning may bring about the animal's death. Otherwise, death must be due to other factors if the development of the reproductive organs is in harmony with the rest of the body. The main study was made on a sample of herrings, called "calf herrings", from the Irish Sea. Each individual was measured, the fish and gonads were weighed separately, and the age was determined by examining the number of annual rings on the scales.* A linear relationship was found between body weight and gonad weight. The testes were somewhat heavier than the ovaries in herrings of comparable size, but the rate of growth of the gonads was practically the same. The relative size of the gonads in relation to the body increased during the first four spawnings but remained constant thereafter. Wynne-Edwards also compared the ratio of gonad weight to body weight for fish of the same weight but of varying ages and learned that the ratio remained constant. He concluded that age was not responsible for any significant change in the weights of the gonad. He states, "There is no indication of an increasing tax which the fish cannot make up, the effects of which continue to pile up until ultimately they cause its death, in a way that has sometimes been suggested". The growth of the gonads was in harmony with that of the other organs.

The question appeared to be settled until Farran (1938) undertook a further study of the Irish herring. He was primarily concerned with the difference in ova diameter between autumn and spring spawners, the latter having larger and less numerous eggs than the former. During the course of the analysis, he related the weight of the ovary and the number of ova in 435 herring to the 4·5 power of the length of the fish, a value greater than the relation of total body weight to

* An age group consists of all fish in a population sample which have the same number of annual rings. A Roman numeral is conventionally used to indicate the number of annual rings.

length. No ages were reported. This relationship was described without rigid statistical treatment, but it is apparent from his diagrams that more refined methods would have produced little change from his value. Farran's formula described the situation except for the largest fish, and it is these that interest us most. The ovary weights and number of ova for these individuals fall below the values predicted by Farran's equation. He recognized this departure and conceded that very large fish show a smaller rate of increase in the size of the ovaries than smaller fish. He interprets this growth pattern in the following way: ". . . that the rate of increase in number (of ova) in fish over 32 cm. in length ceases to correspond to the increase in length and either falls off considerably or ceases altogether." Contrary to Wynne-Edward's conclusions, Farran's results might indicate that reproduction places an increasing strain on the larger female herring, leading to a reduction in number of eggs. On the other hand, Farran may have simply described the normal course of ovary growth in relation to the body.

Sensitive to both of the above workers' findings, Hickling (1940) took up the question, this time using the herring of East Anglia. Both of the previous workers had used only weight of gonads in their analyses. Farran had counted the eggs of only three specimens and used the ratio of number of eggs to ovary weight to calculate egg numbers in the remainder of his sample. Hickling counted the eggs of 136 herring of known age and length, and observed the sex, length, weight, and age of 475 additional individuals.

Hickling agreed with Farran that the rate of gonad growth was greater than the rate of body weight gain in relation to length, and concluded that reproduction became an increasingly greater burden to both male and female as they grew larger and older (Table II). Even more interesting is the fact that the weight of the ovaries increased at a more rapid rate in relation to length ($L^{3.97}$) than the rate of increase in the number of eggs ($L^{3.47}$). This was consistent with his analysis

of the weight of the gonad and egg number as related to age. The rate of increase in gonad weight with respect to age was greater than the rate of increase in egg number. Therefore Hickling was forced to conclude that the permanent tissue of the ovary increases disproportionately as the herring grows larger and older. This suggests a gradual degeneration of the ovary, the reproductive tissues being replaced by connective tissue in much the same manner as the testis changes in *Astyanax mexicanus* in relation to age (Rasquin and Hafter, 1951). Unfortunately, there have been no observations of this sort on the histology of the fish ovary.

Table II

REGRESSIONS OF BODY WEIGHT IN GRAMS (W), GONAD WEIGHT IN GRAMS (GW), AND FECUNDITY (F) ON BODY LENGTH IN CENTIMETRES (L) IN THE ENGLISH HERRING (*Clupea harengus*). TAKEN FROM HICKLING (1940)

	Males	*Females*
Body weight	$W = 0{\cdot}0661\ L^{2{\cdot}312}$	$W = 1{\cdot}1471\ L^{1{\cdot}456}$
Gonad weight	$GW = 2{\cdot}41 \times 10^{-5}\ L^{4{\cdot}237}$	$GW = 5{\cdot}94 \times 10^{-5}\ L^{3{\cdot}973}$
Egg number	... ...	$F = 0{\cdot}2954\ L^{3{\cdot}465}$

Research on the fecundity of the Pacific herring (*Clupea pallasii*) agrees with the conclusions of Hickling and Farran. Katz and Erickson (1950) analysed the relationship of fecundity and length in different age groups. This is a log–log relation described by the formula: $F = CL^n$, where F = fecundity, L = length, and C and n are empirically determined constants. The values of the exponent differed considerably among separate age groups. Those herring that were spawning for the first time (age II) were the least effective egg producers ($n = 3{\cdot}46$). Age groups III and IV were most efficient ($n = 3{\cdot}89$ and $3{\cdot}87$, respectively). The rate of increase in fecundity was considerably less among ages V to VIII ($n = 3{\cdot}52$). This result suggests that the relation of

fecundity to length is not a simple one and can be broken down into three parts, possibly a sigmoid curve. Eschmeyer (1950, 1955) has described a sigmoid fecundity/length relationship in the walleye (*Stizostedion vitreum*) and lake trout. The correlation of a decrease in the rate of egg production with age was regarded by Katz and Erickson as a criterion of ageing in the herring.

A ballot on whether or not the strain of reproduction in the Atlantic and Pacific species of herrings upsets the homeostatic mechanism to the point where the fish dies as a direct or indirect effect of its reproductive efforts yields three votes affirmative, one vote negative. The affirmative votes should be scrutinized carefully, however, because none of them were cast after having taken individual variation into account.

Salmon. Some interesting information has been accumulated which indicates that age influences egg production in two species of salmon. The Atlantic salmon (*Salmo salar*) spawns in rivers after spending either two or three years in the sea and some may spawn more than once. Belding (1940) studied the fecundity of this species from the Gulf of St. Lawrence and learned that the youngest spawners, those which had lived two years in the sea, produced a greater number of eggs in relation to their weight (834 eggs per lb.) than either three-year sea-life individuals (723 eggs per lb.) or those which had previously spawned (738 eggs per lb.). In actual numbers the two-year salmon produced 8,850 eggs per female and the three-year salmon produced about 14,000. He attributed this decline in relative egg production in part to the fact that large salmon usually have larger eggs than small salmon, but he did not discount age as a factor influencing egg production.

Rounsefell (1957) has made a more detailed study of fecundity of the sockeye salmon (*Oncorhynchus nerka*) in the Karluk River, Alaska. In this part of the world the young sockeye spend either three or four years in freshwater lakes before migrating to the sea and remain there either two or three years before returning to freshwater streams to spawn.

Classifying the salmon on the basis of the same freshwater age but different ocean age, Rounsefell pointed out that the older salmon produced a significantly smaller number of eggs than younger ones. The average for the former was 2,987 per female and the average for the latter was 3,285, based on about 150 specimens in each group. The difference in fecundity for sockeye with identical ocean histories but different freshwater ages also favoured the idea that age has an effect on salmon fecundity since the older females produced 118 fewer eggs than the younger ones. The difference was not statistically significant and the data were more variable. The increased variation was explained by the variable freshwater environment as opposed to more stable ocean conditions.

Rounsefell reviews the literature of the fecundity of the family Salmonidae, and of primary interest here is his demonstration that generally the rate of increase in number of eggs declines as the fish increase in size. This may indicate that age influences egg production, or it may be simply a description of the way in which the ovary grows in relation to the rest of the body. It does explain, however, why trout hatcheries discard their old brood stock. The number of eggs in relation to the weight of the fish declines as the fish increase in size, and it is to the hatchery's advantage to have on hand a greater number of smaller breeders than an equal weight of older ones.

Haddock. One of the most penetrating analyses on the effect of age on the fecundity of egg-laying fishes has been done by Raitt (1933). He was also influenced by Orton's writings. The mature eggs of 169 haddock (*Melanogrammus aeglefinis*) of Scottish waters were counted and fecundity was related to length, weight, and age. Four main comparisons were made: (1) rate of increase in fecundity with length, (2) rate of increase in ovary weight with length, (3) rate of decrease in body weight in relation to length during ovarian development, and (4) rate of increase in body weight with length. Comparison of these relationships indicated that fecundity increases with age up to age V, but at older ages

egg production declined (Table III). The values were based on regressions calculated separately for the different age groups. At similar lengths regular increases in fecundity with age occur among ages II, III, IV, and V. Ages VI and VII were combined in the calculations because individuals of

Table III

FECUNDITY OF HADDOCK (*Melanogrammus aeglefinis*) OF THE SAME SIZE AT VARIOUS AGES. MODIFIED FROM RAITT (1933)

Length in cm.	*Age II*	*Age III*	*Age IV*	*Age V*	*Ages VI and VII*
20	11,495				
25	34,255	58,185			
30	83,305	105,150			
35		172,950	181,500	189,410	178,650
40		266,450	283,850	290,900	276,950
45			415,150	424,250	
50			591,600	595,550	
55			809,850	796,600	

these ages were scarce in the population. Their fecundity was about five per cent lower than that of age V. At extreme lengths the latter group has a slightly lower fecundity than age IV of the same length. The same result was found when the fecundity of haddock of the same weight were compared at different ages.

The effect of age was shown to be due to the relationship between fecundity/length and body weight/length. Raitt calculated the first of these comparisons separately for the different age groups. Fecundity increased very rapidly in the youngest spawners of age group II ($F = 0{\cdot}005187 \times L^{4{\cdot}88}$), but was considerably lower in the remainder of the populations, as the remaining equations show: age III ($F = 1{\cdot}788 \times L^{3{\cdot}23}$), age IV ($F = 1{\cdot}527 \times L^{3{\cdot}29}$), age V ($F = 2{\cdot}069 \times L^{3{\cdot}21}$), and ages VI and VII combined ($F = 1{\cdot}546 \times L^{3{\cdot}28}$). Raitt used Russell's extensive data (1914) on the haddock to

compute the rate of increase in body weight with length. Here he found the relationship to be $W = 0{\cdot}0044\ L^{3{\cdot}13}$ based on the mean yearly weights as recorded by Russell. At all ages fecundity increased more rapidly than body weight.

The relationship between fecundity and body weight was: $F = 196 \times W^{1{\cdot}14}$ (all ages). Since the exponent is greater than one, the equation confirmed the above interpretation that fecundity increases at a rate greater than body weight. The rate of increase in ovary weight with length was consistent with this result. The rate of decline in body weight with length during ovarian development showed that somatic tissue was being converted to gonad from November to June, the spawning season, and that somatic tissue increased from July to November.

The consistency of Raitt's results arouses serious suspicion that reproduction is a drain on the individual in later life. In his words, "One cannot but regard the above evidence as hinting at an end point to reproduction, and inviting postulation of stress of egg production, ultimately overbalancing ability to recover within the annual cycle. It would seem that an affirmative answer is suggested to Orton's question of whether 'over-reproduction' may be regarded as a general predisposing cause of death in fishes."

Long rough dab. Bagenal (1957*a*) has recently studied the fecundity of the long rough dab of Scotland by detailed statistical procedures. His fish were caught in one locality by a small mesh cotton trawl. Length, sex, gutted weight, gonad weight, and age were determined for a large series of specimens taken from October 1933 to May 1955. Egg counts and the foregoing measurements were made on two samples, totalling 119 females, one caught in February and the other in March 1954, just before spawning. By an analysis of covariance he was able to show that there was no effect of age on the length/weight regression so all ages were pooled for the calculation of the regression coefficient describing this relationship. Similarly, age had no significant effect on the ovary weight/body

weight regression. There was a significant difference due to age on the ovary weight/length relationship in the March sample, but on good grounds Bagenal considers this to be an anomalous result. Weight increases at a power 3·11 of length in maturing females while ovary weight increases at about the 3·5 power of length. The latter figure is an estimate because the entire data would have to be recalculated in order to obtain an overall coefficient for the two samples. Since the ovary increases at a more rapid rate than body weight, attention is again directed to Orton's theory of "over-reproduction". Whether or not there is a statistical difference between these coefficients would require a separate analysis.

There was no effect of age on fecundity/length or fecundity/weight relationships according to a covariance analysis. Thus differences in these relations could not be attributed to age but to the individual variations that occur in fecundity at any given length or weight. This result makes us more cautious in accepting the rather small decline in fecundity of six- and seven-year-old haddock which Raitt found. He presented no measure of deviations from the regressions, and since the individual measurements were not given the computation cannot be performed.

Even though Bagenal was satisfied with statistical proof that age played no significant rôle in determining ovary weight or fecundity, he was disturbed about two features in his data which did not coincide with this interpretation. Milinsky's (1944) very large dabs from the Barents Sea did not produce the egg numbers expected of their size, based on the Scottish population. The difference might be explained by geographical or by racial variation, which is often very great. Also, the number of eggs did not increase in proportion to the weight of the gonad. The regression coefficients between these two variables are 0·6907 and 0·8117 in his two samples computed from a regression of the logarithm of fecundity on the logarithm of ovary weight. The latter result was, as Bagenal says, " . . . unexpected since the larger gonads will have a

proportionally smaller surface area and so, not only should carry less surface moisture when they are weighed, but also less ovarian tissue should be found surrounding the eggs in the larger gonads. We can only suppose that the heavier gonads produce fewer eggs per gram than do the lighter ones, so the eggs are presumably larger and heavier." It is also possible that the amount of connective tissue of the ovary may increase disproportionately as it grows larger.

After comparing the information on the haddock and long rough dab, we have mixed feelings. Raitt's data were consistent throughout and left the impression that there was a slight but definite effect of age on fecundity although statistical tests were lacking. Bagenal, on the other hand, offers statistical proof to the contrary but cannot explain satisfactorily at least one important feature of his data from a purely biological point of view.

Plaice. A long history is associated with studies on the fecundity of the plaice. Just before the turn of the century Reibisch (1899) completed a detailed study of the histology of the ovary and performed many egg counts on plaice from the Baltic Sea. He was acquainted with the fact that egg production declines with age in higher vertebrates and was puzzled to find that this was apparently not true in fishes. One case was pointed out where an older and larger individual produced the same number of eggs as a younger one. This observation was by no means consistent, and Reibisch was unable to reach a definite conclusion about the effect of age on fecundity.

Soon after, Franz (1909) duplicated Reibisch's work and again was unable to answer the question. Franz admitted that he had insufficient material from older age groups to judge whether older plaice had a greater or lesser egg number than younger ones. Individual variation was very great in the specimens above age X in his sample. The lack of sufficient old specimens has plagued all the studies to date and constitutes the chief source of difficulty in settling the problem.

The older age groups are represented by so few individuals in the population that it is virtually impossible to collect enough material on which to base critical judgments.

A thorough review of plaice fecundity has been done recently by Simpson (1951), who added a considerable number of egg counts from the Southern Bight and Flamborough regions of the North Sea. Ovaries were gathered from a total of 256 females taken just before spawning, from mid-October to mid-February, in 1948 and 1949. By inspecting graphs of the fecundity of plaice of similar lengths against age and graphs of fecundity of fish of the same age against length, Simpson was convinced that age, apart from its relation to size, plays an insignificant part in determining fecundity.

On the chance that statistical analysis might show up differences that a graphical inspection would not, a covariance analysis of Simpson's 1948 sample from Southern Bight (Table IV) was performed. Ages ranging from II to XVI are represented, although it was necessary to lump together ages II and III and ages XII through XVI in order to have sufficient numbers of observations in the younger and older categories. Regressions of body weight on fecundity at each age were calculated and compared. Simpson had found that fecundity bore a linear relation to weight in plaice, thereby simplifying the computations. The regression coefficients ranged from 0·054 to 0·273 and showed no trends with age. No significant differences were found between the regression coefficients or between the adjusted means. Thus we conclude, as Simpson did, that age has no detectable effect on the fecundity of the plaice.

Simpson also measured ovary weights and found a rather high correlation between those and egg number ($r = 0{\cdot}890$). He provided a complete tabulation of his data, and it was possible to make a more detailed study of this relationship. The Southern Bight information was again used, consisting of 163 pairs of observations. Egg number and ovary weights were converted to logarithms and the regression was

calculated to solve the formula: $F = CO_w^n$; where F = fecundity in thousands of eggs; O_w = ovary weight in grams. C and n are empirically determined constants.

The advantage of this computation is that it is possible to judge whether fecundity is increasing in a linear fashion in

Table IV

COVARIANCE ANALYSIS OF REGRESSION OF BODY WEIGHT IN GRAMS AND FECUNDITY IN THOUSANDS OF EGGS IN PLAICE (*Pleuronectes platessa*) OF VARIOUS AGES. CALCULATED FROM DATA OF SIMPSON (1951)

Source of variation	*Degrees of freedom*	*Regression coefficient*	*Mean square from regression*
Age II–III	9	0·099	68·06
IV	35	0·183	238·09
V	8	0·273	146·99
VI	5	0·054	102·19
VII	17	0·117	116·81
VIII	25	0·113	470·47
IX	17	0·148	13648·19
X	9	0·138	1017·94
XI	11	0·098	828·72
XII–XVI	11	0·164	453·74
Within age groups	147		481·98
Due to regression	9		899·11
Common to all age groups	156	0·140	506·04
Due to adjusted means	9		605·99
Total	165		511·50

F for regression coefficients: $\frac{899 \cdot 11}{481 \cdot 98} = 1 \cdot 87$ (not significant)

F for adjusted means: $\frac{605 \cdot 99}{506 \cdot 04} = 1 \cdot 20$ (not significant)

relation to ovary weight or whether it is increasing more rapidly or less rapidly. The exponent, n, would not deviate significantly from 1 in the first case, would be < 1 in the second, and > 1 in the third. The solution of the equation was: $F = 7 \cdot 14\ O_w^{0 \cdot 5794}$ with 95 per cent confidence limits of

the exponent lying between 0·5553 and 0·6035. Thus, the number of eggs does not increase in proportion to the weight of the ovary (Fig. 2).

Plaice is the fourth species to show this peculiar relationship. It had also been reported by Hickling in the English herring, by Raitt in haddock and by Bagenal in the long rough dab.

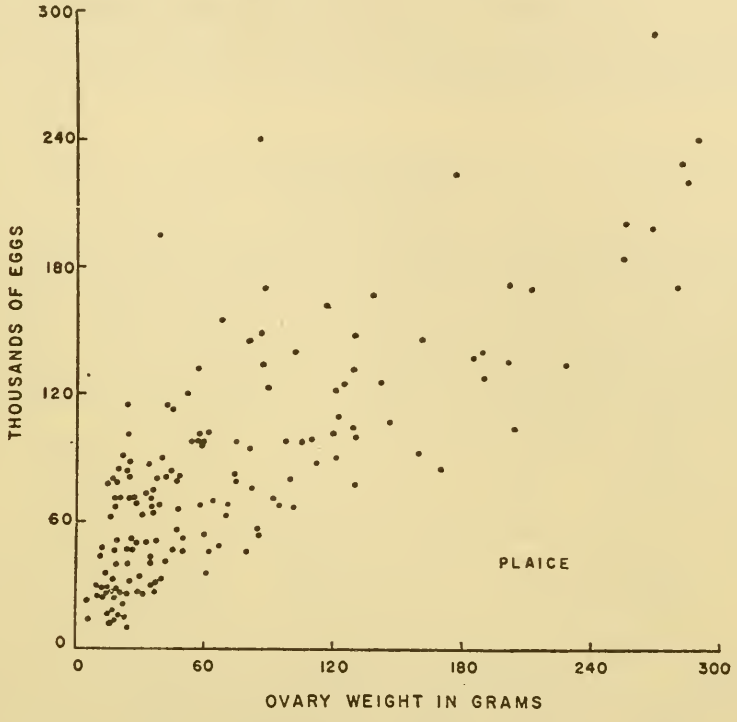


FIG. 2. Scatter diagram of the relation between fecundity and ovary weight in the plaice (*Pleuronectes platessa*). From Simpson (1951).

The explanation for it is still in doubt, but a clear-cut problem has emerged. A choice can be made between Bagenal's interpretation that larger ovaries may produce larger but fewer eggs, and Hickling's tentative conclusion that connective tissue may increase disproportionately in the ovaries of older fish. The decision can be made by studying the histology of the ovary, provided a method can be devised for measuring

the relative amounts of connective tissue. This would have to be done in maturing ovaries where maximum egg diameters could be measured at the same time.

There seems to be no reason to continue studying fecundity of egg-laying fishes with respect to age for gathering evidence for or against the ageing process. Individual variation masks any effect that age may have. Great variation plus the difficulty in collecting a sufficiently large number of old individuals makes it very improbable that this line of research will ever become profitable.

Summary

Nutrition and reproduction of fishes are reviewed in relation to age. A decline in the ability to utilize protein for growth is exhibited as fish grow larger and older. This conclusion is based on laboratory feeding experiments on the longear sunfish (*Lepomis megalotis*), green sunfish (*Lepomis cyanellus*), bluegill sunfish (*Lepomis macrochirus*), and red hind (*Epinephalus guttatus*). Other vertebrates also conform to this pattern, although they achieve a specific size relatively early in life in contrast to the prolonged period of growth in fishes.

The reproductive capacity of live-bearing fishes of the family Poeciliidae declines with age and there may be a period of sterility before death. These results were obtained by field observations and laboratory experiments on the fecundity of the western mosquitofish, *Gambusia affinis*. Scattered observations among other species in the family agree with this viewpoint.

The effect of age on fecundity in egg-laying fishes is not yet clear. The number of eggs in three-year sea-life sockeye salmon (*Oncorhynchus nerka*) is significantly lower than in two-year individuals. The same general phenomenon has been said to be true of haddock (*Melanogrammus aeglefinis*), but there is some doubt about this conclusion since statistical

procedures fail to show any effect of age on the fecundity of either the long rough dab (*Hippoglossoides platessoides*) or plaice (*Pleuronectes platessa*). Individual variation in fecundity is very great and masks any effect that age may have.

Ovary weight and fecundity increase more rapidly in relation to length than does body weight in the long rough dab, haddock, and herring (*Clupea harengus* and *Clupea pallasii*). This result strengthens Orton's hypothesis that reproduction becomes an increasing strain on the metabolism of fish as they grow larger and older, thereby causing death either directly or indirectly.

The number of eggs does not increase in proportion to the weight of the ovary in the haddock, dab, herring, or plaice. Either larger ovaries produce larger and fewer eggs or connective tissue increases disproportionately in the ovaries of larger fish. No critical evidence is available to support either contention. If the latter is true, ageing changes in the gonads of fishes would be similar to those in higher vertebrates.

REFERENCES

BAGENAL, T. B. (1957*a*). *J. Mar. biol. Ass. U.K.*, **36**, 339.
BAGENAL, T. B. (1957*b*). *J. Mar. biol. Ass. U.K.*, **36**, 377.
BELDING, D. L. (1940). *Trans. Amer. Fish. Soc.*, **67**, 285.
BIDDER, G. P. (1925*a*). *Nature* (*Lond.*), **115**, 155.
BIDDER, G. P. (1925*b*). *Nature* (*Lond.*), **115**, 495.
BIDDER, G. P. (1932). *Brit. med. J.*, **2**, 583.
DAVIS, W. S. (1957). *Res. Rep. U.S. Fish Serv.*, **49**, 1.
ESCHMEYER, P. H. (1950). *Bull. Inst. Fish. Res. Univ. Mich.*, **3**, 7.
ESCHMEYER, P. H. (1955). *Trans. Amer. Fish. Soc.*, **84**, 47.
FARRAN, G. P. (1938). *J. Cons. int. Explor. Mer*, **13**, 91.
FRANZ, V. (1909). *Wiss. Meeresuntersuch.* (*Abt. Helgoland*), **9**, 59.
FRASER, E. A., and RENTON, R. M. (1940). *Quart. J. micr. Sci.*, **81**, 479
FRY, F. E. J. (1949). *Biometrics*, **5**, 27.
GERKING, S. D. (1952). *Physiol. Zoöl.*, **25**, 358.
GERKING, S. D. (1954). *Ecology*, **35**, 490.
GERKING, S. D. (1955*a*). *Physiol. Zoöl.*, **28**, 267.
GERKING, S. D. (1955*b*). *Physiol. Zoöl.*, **28**, 283.
HICKLING, C. F. (1940). *J. Mar. biol. Ass. U.K.*, **24**, 619.
IVLEV, V. S. (1939*a*). *C.R. Acad. Sci. U.R.S.S.*, **25**, 87.

IVLEV, V. S. (1939*b*). *Bull. Soc. Nat. Moscou*, **48**, 70.
IVLEV, V. S. (1939*c*). *C. R. Acad. Sci. U.R.S.S.*, **25**, 90.
JUNE, F. C. (1953). *Fish. Bull., U.S.*, **77**, 47.
KARZINKIN, G. S. (1939). *Arb. limnol. Sta. Kossino*, **22**, 219.
KATZ, M., and ERICKSON, D. W. (1950). *Copeia*, p. 176.
KRUMHOLZ, L. (1948). *Ecol. Monogr.*, **18**, 1.
LARKIN, P. A., TERPENNING, J. G., and PARKER, R. R. (1957). *Trans. Amer. Fish. Soc.*, **86**, 84.
MCGREGOR, E. A. (1923). *Calif. Fish Game*, **8**, 138.
MÄÄR, A. (1949). *Rep. Inst. Freshw. Res. Drottning.*, **29**, 57.
MAYNARD, L. A. (1951). Animal Nutrition, 3rd ed. New York: McGraw-Hill.
MENZEL, D. W. (1957). Ph.D. Thesis, University of Michigan.
MILINSKY, G. I. (1944). *Trans. Knipovich polyar. sci. Inst.*, **8**, 388.
MORGULIS, S. (1919). *Trans. Amer. Fish. Soc.*, **48**, 34.
ORTON, J. H. (1929). *Nature (Lond.)*, **123**, 3088.
RAITT, D. S. (1933). *Rep. Fish. Bd. Scot.*, p. 1.
RASQUIN, P., and HAFTER, E. (1951). *J. Morph.*, **89**, 397.
REIBISCH, J. (1899). *Wiss. Meeresuntersuch. (Abt. Kiel)*, **4**, 233.
ROUNSEFELL, G. A. (1957). *Fish. Bull., U.S.*, **122**, 451.
RUSSELL, E. S. (1914). *Fish. Invest., Lond., Ser.* 2, **1**.
SIMPSON, A. C. (1951). *Fish. Invest., Lond., Ser.* 2, **17**, 3.
SVÄRDSON, G. (1949). *Rep. Inst. Freshw. Res. Drottning.*, **29**, 115.
SVÄRDSON, G. (1951). *Rep. Inst. Freshw. Res. Drottning.*, **32**, 79.
WALLACE, W. (1925). *Nature (Lond.)*, **115**, 337.
WYNNE-EDWARDS, V. C. (1929). *J. Mar. biol. Ass. U.K.*, **16**, 49.

DISCUSSION

Comfort: We have done some work on regeneration in guppies (Comfort, A., and Doljanski, F. (1958). *Gerontologia (Basel)*, **2**, 266) which might have some relevance to what you said about protein utilization, Dr. Gerking. We cut off the tips of the tails and measured the percentage restoration in length at various times. In female guppies up to three years of age the growth curves were typically asymptotic, and the corresponding curve for percentage restoration of an excised regenerate was roughly a mirror image of them. In fish that had been kept without much to eat, the growth curve flattened out and the regeneration rate fell exactly as in freely growing fish approaching full size. Full-size and retarded brood-mates were therefore behaving in almost the same way as regards regeneration. If retarded fish are then allowed to grow, the rate of regeneration rises until growth declines again. In other words, as the asymptote for size under given conditions is approached, the

regeneration rate falls with the growth rate. Growth eventually declines to zero, and the regeneration rate to its basal level, which persists even in starving fish.

Danielli: Are these measurements in terms of percentage regeneration of what was removed ?

Comfort: Yes. They are not absolute measurements. We had to adjust the size of the amputate to the size of the fish. The general finding seems to be that as somatic growth flattens out, the regeneration rate comes down to its basic level; as growth is restarted, so regeneration is restarted. I would predict that this occurs also with nitrogen utilization, as in Dr. Gerking's experiments.

As G. V. Samokhvalova has shown (1952. *J. gen. Biol., Moscow*, **12**, 153), in guppies during the first part of life the number of young per brood is a function of the size of the female. I have kept them up to four and a half years of age. Brood size declines fairly rapidly even though body growth continues, and there is quite a long post-reproductive period during which females may produce one or two broods if remated, but generally they do not.

Gerking: It seems that my paper would have been much more complete if your experiments had been published a little earlier.

Holt: Some light could probably be thrown on the regeneration question if the growth could be modified not just by changing the food supply, but also by changing the temperature. You could then see whether the regeneration curves behaved in the same way. In our terminology your food supply is changing the L_∞ (the asymptotic size), whereas the temperature would change K (the rate of approach to the asymptote).

Comfort: I am now engaged in temperature experiments. If two batches of fish are allowed to regenerate at different temperatures the final percentage restoration is identical, but it is reached at a different rate. It is striking that, as far as I have got, quite large shifts in temperature do not alter the final percentage of restoration; they only alter the rate at which it is approached, as you suggested, Mr. Holt.

Rotblat: One of your graphs [not printed] appears to be the differential of the other.

Comfort: In general but not invariably. If very old retarded fish are kept very long, as is often the case, some of them will not restart growth. They grow only very sluggishly or very little. Nevertheless the regeneration rate still rises.

Rotblat: Even when there is a small change in weight, the initial slope appears to increase.

Comfort: Some of them do not increase at all or show barely

measurable growth. But even in these the regeneration rate rises, and I would suggest that the nitrogen uptake rises too.

Rotblat: Does this mean that the rate of restoration equals the rate of growth?

Comfort: The response of regeneration to a growth-promoting stimulus is more sensitive than that of body growth. That is why I would not like to say that regeneration rate is a direct function of growth rate.

Gerking: Do your findings apply to the male ?

Comfort: No; the male guppy not only stops growing rather suddenly and early, but also it has tail shapes of different kinds. As far as we have got, in males with small, wild-type tails the percentage regeneration falls in relation to growth cessation, as in females, but the basic restoration rate always stays higher than in the female. You sometimes find male guppies of all ages which for some reason have not quite completed their growth and which have a very high restoration rate. In strains with big tails, it appears that the rate of restoration is based, as it were, on the wild-type tail, but that anything after that is extra.

Holt: Dr. Gerking, you have looked at particularly good sets of data and put aside the incomplete oddments. I have had a look at the oddments and have the impression that although no single species shows a statistically significant decline in fecundity (eggs per gram) with increase in size, yet in many cases the points for the larger fish fall below the proportional line.

Gerking: That is very true. I am not convinced whether the decrease is significant or not.

Holt: In this kind of study you may be seeing the effects of less fecund fish surviving longer. What we cannot do is to follow a cohort. We need a method of determining the fecundity of live individuals and marking them.

Rockstein: Was this large longear sunfish that utilized very little protein caught at a great depth, Dr. Gerking ?

Gerking: No, it was caught in a shallow stream. This observation needs to be confirmed, and I do not wish to over-emphasize that portion of Fig. 1. It may indicate that extremely old fish utilize very little protein for growth.

Nigrelli: In the experiments carried out in Bermuda on the angelfish you characterize these fish as herbivores.

Gerking: We have thought up to this time that they were herbivores; it is known that they feed upon algae because algae can be found in the gut. Menzel's experiments (1957), however, indicate that if they are fed exclusively on algae they will not grow, even if

they eat fairly large quantities. I would conclude that these angelfish are not strict herbivores but that they must have some animal food.

Nigrelli: That is true, because we keep small angelfish in our aquarium and feed them with clams, etc., and no algae at all, and they grow to a good size. However, the algae may prevent growth by producing antibiotics.

Gerking: We wonder now whether there is a strictly herbivorous fish.

LONGEVITY OF FISHES IN CAPTIVITY, WITH SPECIAL REFERENCE TO THOSE KEPT IN THE NEW YORK AQUARIUM

Ross F. Nigrelli
New York Aquarium

The New York Aquarium, at one time or another during its history, has exhibited for varying periods of time fishes representing 33 of the 57 known orders. This figure is more spectacular when it is realized that 10 of the 57 orders contain species restricted to life in the benthic areas of the seas, which have never been brought to the surface alive long enough to exhibit. The orders, as listed by Berg (1947), contain 425 families, at least 50 of them deep-sea forms. The New York Aquarium has exhibited species representative of 152 families. Other aquaria have probably kept fishes of another five or six orders, involving an additional 25 families. Therefore, it is apparently possible to maintain in captivity fishes representing 38 of the 57 orders and from 175–250 of the 425 families. However, only relatively few of the estimated 25,000 species have ever been captured and kept alive in aquaria; the exact number has never been determined. Jordan, Evermann and Clark (1930) list 4,137 species in the North and Middle American waters, and probably only a little more than one-fourth of these have ever been exhibited. Breder (1936*b*) summarizes some of the environmental and physiological barriers that may be limiting factors for the successful maintenance of many species. He concedes, however, that these barriers may be overcome and that some day it may be possible to exhibit species not heretofore shown, including the exotic life in the great depths of the oceans.

It is generally known that fishes represent a physiologically highly diversified group of vertebrates, and attempts to maintain them in so-called standard aquarium conditions regardless of environmental origin are fraught with danger and will invariably be reflected in a short lifespan in captivity. As environmental origin is recognized as important in aquarium management, it is the practice in the New York Aquarium, in so far as it is possible, to diversify physical and chemical conditions such as temperature, pH, surface-volume ratios, conditioning factors, water movements, salinity and illumination. As a result of such management we have been able to increase our survival rates significantly. Thus, in 1940, our last full year of operation at the New York Aquarium at the Battery, average longevities were as follows: marine fishes 9·58 months, temperate freshwater species 24·50 months, and tropical freshwater fishes 11·22 months. The mortality rate for the year was 169 per 1,000.

Infectious diseases are the primary causes of death in aquaria (Nigrelli, 1940, 1943). It is generally known that fishes are susceptible to a large variety of metazoan parasites, but what is not common knowledge is that they are also prone to infections by pathogenic micro-organisms that are similar in many respects to those responsible for diseases in man and other mammals. For example, to mention a few, fishes are susceptible to infections by viruses, *Rickettsia*, *Pseudomonas*, *Proteus*, diphtheroids, tubercle bacilli (*Mycobacterium*), *Monilia* and other mycotic organisms. They are also susceptible to such protozoans as trypanosomes, haemogregarines, coccidians, babesioids, and *Toxoplasma*, in addition to such ubiquitous parasites as flukes, tapeworms, nematodes and acanthocephalans. The most important aetiological agents of fish diseases, however, belong to a subclass of Sporozoa called cnidosporidians. These are truly spore-producing parasites in which transmission is direct, i.e. by ingestion of the spore. During the course of routine autopsies at the New York Aquarium in the last 25 years, the present

author has observed more than 150 species of cnidosporidians (myxo- and microsporidians) in more than 1,000 species of fishes (see Walford, 1958). These parasites are often tissue- and cell-specific and have been found in all the tissues and organs, including the eyes, brain and heart. The parasites produce a variety of lesions, the extent of which varies with the species of parasite and degree of infection. They may cause no more damage than the development of a simple cyst, or they may cause acute and chronic diseases. For example, some may produce cellulitis, cystitis, nephritis, hepatitis, enteritis, pericarditis and endocarditis; others may induce tumours of the infected organs and/or the surrounding tissues, many of them bordering on true neoplasia; still others may cause hyaline degeneration of muscle and other tissues.

It is safe to say that all fish harbour one or more kinds of parasites. The resistance of fish, or the rate at which they can acclimatize to changes in the environment, appears to be related to their parasitic load. Experience has shown that as a rule a 10 per cent mortality can be expected when fish are first netted or trapped randomly, another 10 per cent as the result of handling and shipment, and 10 per cent more will succumb in the first few weeks of life in the tanks. Such fish tend to show a relatively high degree of parasitaemia, and their ability to withstand shock is related to the intensity and the site of infection or infestation, the rates being highest for those fish in which infections are localized in the kidneys, gills and skin, which are important organs of osmoregulation. Selective methods of trapping, handling and shipping usually result in higher survival values. For example, fish caught in traps rather than in nets are less subject to trauma and can be transferred to holding-pens with very little injury. Survival rates are further increased if the fishes are starved for a period of time and before shipping are transferred to waters with slightly altered densities. Relatively young fish, as related to potential age, are better risks than yearling or older (larger) fish.

Conditions in aquaria at best are still artificial since movements of fishes are restricted, and for this reason there cannot be any escape from environmental stress. It is apparent, then, that fishes that survive aquarium conditions are those that can withstand shock stresses and can acclimatize to a variety of exaggerated environmental factors. But even such fish as these are often at the limits of their tolerance, and any sudden change in one or more of the physical, chemical and biological factors often results in death or increased susceptibility to infections. Invariably these infective agents are external (gill and skin) protozoan and helminthic parasites; only rarely are they bacterial or mycotic organisms. This would indicate that once the fish is acclimatized to its new environment (captivity), its resistance is increased and the parasite load diminished to a point where immunity is maintained by premunition. Diseases caused by internal parasites are often self-limiting and in some instances may spontaneously disappear.

Once a balance has been established between fish, parasites and environment, other diseases of a non-infectious nature may develop. It may not be surprising that the greatest single cause of mortality is associated with nutrition. Fishes, like other animals, are herbivorous, carnivorous and omnivorous and all need an exogenous source of vitamins and other nutriments. The main food source in the New York Aquarium consists chiefly of commercial-grade fresh and frozen fish, clams and crustacea. The kind of fish used for feeding depends entirely on their availability on the market and in collecting areas. Feeding oily fish (mackerel, herring, etc.) over relatively long periods to species that normally eat invertebrates and non-oily fish frequently results in liver damage, commonly referred to as fatty degeneration but properly called fatty "metamorphosis" or "fatty change". The pancreas, kidneys and other organs may also be involved in this type of damage. Fatty changes may be due to a relative anoxia, the result of prolonged passive congestion. Other diseases of fishes indicative of disturbances in carbohydrate

and protein metabolism are glycogen storage comparable to von Girke's disease in man, cloudy swelling (albuminous degeneration), hydropic degeneration and amyloidosis of the liver and kidney, to mention a few. The development of melanosis, a common disturbance in fishes generally, certainly indicates profound changes in metabolism involving the amino acids phenylalanine and tyrosine, and the excessive accumulation of guanine crystals in the tissues of certain marine species in captivity is indicative of disturbance in purine metabolism.

Further, it should also be emphasized that fishes are susceptible to neoplasia (Nigrelli, 1952, 1954*a*). With the possible exception of typical leukaemias, all types of tumours and cancers, benign and malignant, occur in fish. The same basic tissues as in mammals are involved, with tumours of mesenchymal origin predominating. Although we do not have definite age statistics, there is ample evidence that such abnormal growths occur more frequently in older fish. This is especially true for sarcomas and lymphomas, basic tumour types that appear more frequently in young persons. This finding, together with the fact that tumours in fish are usually slow-growing, may have some physiological and phylogenetic significance.

It serves no purpose here to extend the list of metabolic diseases that we have found in fishes in captivity. The vertebrate fish is no different from vertebrate man in these respects. It is sufficient to say that we have ample evidence that some of the metabolic diseases may be hereditary or congenital in origin, or that, in older fishes at least, they may result from nutritional disturbances and hormonal imbalances. The pathological changes are generally similar to those found in warm-blooded vertebrates; in extreme cases they include hyperaemia, anaemia, haemorrhage, inflammation, sclerosis, atrophy, hypertrophy, hyperplasia, oedema, ascites and necrosis. Basically, such conditions result in disturbances in the electrolyte balance, thus affecting homeostasis.

The literature concerning growth and senescence in fishes has been reviewed by Comfort (1956) and Brown (1957) and it is generally agreed that many of the larger teleosts, and perhaps certain sharks, continue to grow throughout life. Most fishes, however, reach their maximum growth, often with sexual maturity, within a limited time. Nevertheless, the growth pattern and lifespan of only a relatively few but well-known species have been established by fishery biologists. The lifespan of the more exotic forms is based mainly on longevity records kept by various aquaria. These, and others, have been summarized by Flower (1925, 1935), Bourlière (1946), and more recently by Hinton (1959, personal communication). In 1956 Hinton canvassed twenty institutions in Europe and the United States for information concerning longevity of fishes in attempts to bring these records up-to-date. The New York Aquarium's longevity lists for fishes 4 years or over are included in this report as Tables II, III and IV. The data were obtained from published papers by Townsend (1904, 1913, 1928*a*, *b*), Mellen (1919, 1925), Breder (1936*a*), Nigrelli (1940, 1954*b*) and from our own mortality records not previously published. In the most recent listing by Hinton, 325 species had lifespans of 5 years or more and these belong to 88 families. A further analysis of his data shows the following: 64 families contained 93 species with lifespans from 5 to 9 years, 11 months; 43 families contained 108 species that lived from 10 to 19 years, 11 months; and 18 families contained 28 species that lived more than 20 years. The latter group is listed in Table I. Families with the largest number of species that lived for 5 years or more are Characidae, 37 species; Cyprinidae, 39 species; Serranidae, 28 species; Sparidae, 12 species and Cichlidae, 17 species. The two orders represented by these families are Cypriniformes and Perciformes. Forty-four of the 88 families are represented by single species and the other families by two to nine species.

A casual examination of all published lists of long-lived fishes in captivity shows, with few exceptions, the following

general characteristics: (1) they are phylogenetically primitive, (2) they are sluggish in their movements, (3) they are bottom inhabitants or live in fairly shallow waters, (4) they have accessory respiratory devices, (5) they can aestivate or hibernate, (6) they live in regions of extreme sunlight, (7) they are adapted to live in environments with low oxygen concentration (less than 5 p.p.m.), and (8) they are adapted to environments with extreme fluctuations in temperatures and salinities. The significance of some of these factors may not be apparent. For example, there seems to be some correlation between longer daylight and decreased respiratory rates, especially in fishes kept above 15°. Also, fishes that live on some coral reefs and banks no doubt are acclimatized to great changes in temperature and salinities. Certain "reef" fishes can even survive in fresh water, provided the calcium content is high. Thus, Breder (1934) reports 12 typically marine species that he found living in a freshwater lake (Lake Forsyth) on Andros Island, British West Indies. Further, experience has shown that many marine tropical species survive longer in captivity if the sea water is reduced in salinity to around 30 parts per thousand.

Although there is much evidence that fishes (teleosts) undergo reproductive and actuarial senescence, there is very little information in the literature relative to pathological changes associated with ageing. Rasquin and Hafter (1951) and Hafter (1952) reported age changes in the testes and thymus of the teleost, *Astyanax mexicanus*. From the clinical records of the New York Aquarium, in addition to gonad atrophy we have found the following pathological manifestations to be most frequently associated with ageing: cirrhosis and fatty changes in the liver and kidneys, haemochromatosis, hypochromic anaemia, degeneration of the mucus-producing glands of the skin, hyperostosis of the haemal arch bones (see Breder, 1952) and other vertebral abnormalities. The haemochromatosis and anaemia are the direct result of changes in the kidney and spleen, important

Table I

EXCEPTIONALLY LONG-LIVED FISHES*

Order	*Family*	*Species*	*Yrs.*	*Mos.*	*Institution*
LAMNIFORMES	Orectolobidae	*Ginglymostoma cirratum*	25		Chicago Aquarium
RAJIFORMES	Trygonidae	*Dasyatis pastinaca*	21		London Aquarium
CERATODIFORMES	Ceratodidae	*Neoceratodus forsteri*	22	4	Chicago Aquarium
LEPIDOSIRENIFORMES	Protopteridae	*Protopterus annectens*	23		New York Aquarium
POLYPTERIFORMES	Polypteridae	*Polypterus senegalus*	34		Giza Zool. Gard., Egypt
ACIPENSERIFORMES	Acipenseridae	*Acipenser fluvescens*	23	3	Chicago Aquarium
		A. ruthenus	69	8	Amsterdam Aquarium
AMIIFORMES	Amiidae	*Amia calva*	30		New York Aquarium
LEPIDOSTEIFORMES	Lepidosteidae	*Lepidosteus osseus*	30		New York Aquarium
		L. platostomus	20		New York Aquarium
		L. spathula	23	4	Chicago Aquarium
MORMYRIFORMES	Mormyridae	*Marcusenius isidori*	28	11	(see Flower, 1935)
CYPRINIFORMES	Characidae	*Serrasalmus niger*	21	4	Chicago Aquarium
	Synodontidae	*Synodontis schall*	31		(see Flower, 1935)
	Cyprinidae	*Cyprinus carpio*	38		Frankfort Aquarium
		Leuciscus idus	21	7	Amsterdam Aquarium
		Scardinius erythrophthalmus	20	3	Chicago Aquarium
	Doradidae	*Doras* sp.	26	5	Amsterdam Aquarium
	Pimelodidae	*Pimelodus clarias*	27	1	Amsterdam Aquarium
		P. stegelichi	30	8	Amsterdam Aquarium
ANGUILLIFORMES	Muraenidae	*Gymnothorax funebris*	20	4	Chicago Aquarium
		G. mordax	26		Scripps Inst., Calif.
		Muraena helena	20	3	Amsterdam Aquarium
PERCIFORMES	Serranidae	*Roccus saxatilis*	24		New York Aquarium
		Morone labrax	30		Amsterdam Aquarium
		Epinephelus gigas	29	2	Monaco Aquarium
	Eleotridae	*Eleotris marmoratus*	20	5	Amsterdam Aquarium
MUGILIFORMES	Mugilidae	*Mugil chelo*	23		Plymouth Aquarium

* From records of the New York Aquarium and from those compiled by S. Hinton.

Table II

Longevity of fishes in the New York Aquarium

Marine Species
(Four years or more)

Order	*Family*	*Species*	*Common name*	*Yrs.*	*Mos.*
Lamniformes	Orectolobidae	*Ginglymostoma cirratum*	Nurse Shark	6	
	Odontapsidae	*Odontapsis littoralis*	Sand Shark	9	
Rajiformes	Myliobatidae	*Rhinoptera quadriloba*	Cow-nosed Ray	4	
Acipenseriformes	Acipenseridae	*Acipenser brevirostrum*	Short-nosed Sturgeon	7	
Clupeiformes	Megalopidae	*Tarpon atlanticus*	Tarpon	4	8
Cypriniformes	Ariidae	*Galeichthys felis*	Sea Catfish	7	
Gasterosteiformes	Gasterosteidae	*Apeltes quadracus*	Four-spined Stickleback	4	
Cyprinodontiformes	Poeciliidae	*Fundulus heteroclitus*	Common Killifish	4	
Beryciformes	Holocentridae	*Holocentrus adscenionis*	Squirrel Fish	5	
Perciformes	Serranidae	*Roccus saxatilis*	Striped Bass	24	
		Mycteroperca venenosa	Yellow-fin Grouper	5	
		M. v. apua		5	
		M. bonaci	Black Grouper	5	
		M. interstitialis	Princess Rockfish	4	
		M. tigris	Tiger Rockfish	5	
		Epinephelus morio	Red Grouper	7	
		E. striatus	Nassau Grouper	7	
		E. guttatus	Red Hind	7	
		Promicrops itaiara	Giant Grouper	12	
		Centropristis striatus	Black Sea Bass	4	
		Morone americana	White Perch	7	
	Carangidae	*Caranx hippos*	Common or Horse Jack	5	
		C. crysos	Hard-tailed Jack	5	
		Trachinotus falcatus	Round Pompano	4	6
		T. carolinus	Common Pompano	4	2
		T. glaucus	Palometa	5	

		Selene vomer	Look-down	5	
		Vomer setapinnis	Moonfish	4	6
		Naucrates ductor	Pilotfish	4	
		Seriola dumerili	Amber Jack	4	6
		S. zonata	Rudder Fish	4	
	Lutianidae	*Lutianus jocu*	Dog Snapper	14	7
		L. griseus	Gray Snapper	7	
		L. synagris	Spot Snapper	7	
		Ocyurus chrysurus	Yellowtail	4	
	Pomadasyidae	*Haemulon sciurus*	Blue-striped Grunt	5	
	Sciaenidae	*Pogonias cromis*	Drum	6	6
		Sciaenops ocellatus	Channel Bass	7	
		Cynoscion regalis	Weakfish	5	
	Sparidae	*Stenotomus chrysops*	Porgy	4	4
		Archosargus probatocephalus	Sheepshead	6	
	Kyphosidae	*Kyphosus secatrix*	Bermuda Chub	4	
	Ephippidae	*Chaetodipterus faber*	Spadefish	10	
	Seatophagidae	*Scatophagus argus*	Scat	4	
	Chaetodontidae	*Angelichthys isabelita*	Blue Angelfish	5	
		Heniochus sp.	Long-finned Butterfly Fish	4	
	Cichlidae	*Tilapia mossambica*		5	
	Labridae	*Tautogolabrus adspersus*	Cunner	4	
		Tautoga onitis	Blackfish	8	
		Halichoeres radiatus	Pudding-wife	4	
		Thalassoma bifasciatus	Blue-head	4	
	Acanthuridae	*Acanthurus hepatus*	Doctor Fish	5	
TETRODONTIFORMES	Balistidae	*Balistes carolinensis*	Common Trigger Fish	5	
		Canthidermis sabaco	Ocean Trigger Fish	4	
	Ostraciidae	*Lactophrys tricornis*	West Indian Cowfish	4	
		Lactoria sp.	East Indian Cowfish	4	
	Tetrodontidae	*Sphaeroides maculatus*	Puffer	4	
	Diodontidae	*Diodon hystrix*	Porcupine Fish	4	
BATRACHOIDIFORMES	Batrachoididae	*Opsanus tau*	Toadfish	5	

Table III

Longevity of fishes in the New York Aquarium

Temperate Freshwater Species
(Four years or more)

Order	*Family*	*Species*	*Common name*	*Yrs.*	*Mos.*
Acipenseriformes	Acipenseridae	*Acipenser brevirostrum*	Short-nosed Sturgeon	7	
		A. oxyrhynchus	Common Sturgeon	5	
		A. rubicundus	Lake Sturgeon	4	
		A. fulvescens	Lake Sturgeon	5	
		Scaphirhynchus platorhynchus	Shovel-nosed Sturgeon	5	
Amiiformes	Amiidae	*Amia calva*	Bowfin	30	
Lepidosteiformes	Lepidosteidae	*Lepidosteus osseus*	Long-nosed Gar	30	
		L. platostomus	Short-nosed Gar	20	
Clupeiformes	Salmonidae	*Oncorhynchus tshawytscha*	Chinook Salmon	4	
		Salmo gairdneri	Steelhead Trout	4	
		S. g. irideus	Rainbow Trout	4	
		S. fario	Brown Trout	5	
		Salvelinus fontinalis	Brook Trout	5	
	Coregonidae	*Coregonus clupeaformis*	Whitefish	12	
		Prosopium quadrilaterale	Round Whitefish	5	
	Esocidae	*Esox masquinongy*	Muskallunge	10	
		E. lucius	Northern Pike	6	
Cypriniformes	Catastomidae	*Carpiodes velifer*	Quillback	4	
	Cyprinidae	*Scardinius erythrophthalmus*	Pearl Roach	12	

		Notemigonus crysoleucas	Golden Shiner	10	
		Rhinichthys atratulus	Black-nosed Dace	5	
		Idus idus	Ide	7	
		Tinca tinca	Tench	7	
		Carassius auratus	Goldfish	10	
	Ictaluridae	*Ictalurus furcatus*	Blue Catfish	4	6
		I. punctatus	Channel Catfish	5	
		I. lacustris	Northern Channel Catfish	5	
		I. nebulosus	Brown Bullhead	5	
		Pylodictis olivaris	Mud Catfish	6	2
ANGUILLIFORMES	Anguillidae	*Anguilla rostrata*	Common Eel	6	
GADIFORMES	Gadiidae	*Lota lota*	Burbot	5	
GASTEROSTEIFORMES	Gasterosteidae	*Eucalia inconstans*	Brook Sticklebaek	4	
PERCIFORMES	Percidae	*Perca flavescens*	Yellow Perch	12	
	Centrarchidae	*Micropterus dolomieui*	Small-mouth Bass	11	
		M. salmoides	Large-mouthed Bass	7	
		Lepomis auritis	Red-breasted Sunfish	4	
		L. megalotis	Long-eared Sunfish	4	
		L. humilis	Red-spotted Sunfish	4	
		L. macrochirus	Blue-gill Sunfish	8	2
		L. gibbosus	Common Sunfish	4	
		Ambloplites rupestris	Rock Bass	18	
		Pomoxis nigromaculatus	Calico Bass	12	
	Serranidae	*Morone americana*	White Bass	5	
		M. interrupta	Yellow Bass	5	
	Cottidae	*Cottus gracilis*	Miller's Thumb	5	

Table IV

LONGEVITY OF FISHES IN THE NEW YORK AQUARIUM

Tropical Freshwater Species
(Four years or more)

Order	*Family*	*Species*	*Common name*	*Yrs.*	*Mos.*
LEPIDOSIRENIFORMES	Protopteridae	*Protopterus annectens*	African Lungfish	23	
CYPRINIFORMES	Characidae	*Astyanax bimaculatus*		4	
		Hyphessobrycon rosaceus	Rosy Tetra	4	
		H. serpae		5	
		H. heterorhabdus		5	
		Moenkhausia oligolepis		4	
		Pristella riddlei		5	
		Serrasalmus scapularis		5	
		Nannaethiops unitaeniatus	One-striped African Characin	5	
		Moenkhausia pittieri		4	
	Gymnotidae	*Gymnotus coatesi*	Coates' Knifefish	4	
	Electrophoridae	*Electrophorus electricus*	Electric Eel	6	
	Cyprinidae	*Rasbora trilineata*	Three-lined Rasbora	4	
		R. danicona	Slender Rasbora	5	
		Esomus malayensis	Malayan Flying Barb	4	
	Malapteruridae	*Malapterurus electricus*	Electric Catfish	7	
CYPRINODONTIFORMES	Poeciliidae	*Belonesox belizanus*	Pike-killie	4	6
OPHIOCEPHALIFORMES	Ophiocephalidae	*Channa asciatica*	Snake-head	6	6
PERCIFORMES	Cichlidae	*Etroplus maculatus*	Orange Chromide	6	
		Ctenops vittatus	Croaking Gourami	4	

organs of haemopoiesis. Fishes with these abnormalities may live for an exceptionally long time, even when the kidneys are extensively damaged, since the osmoregulation function of this organ can be taken over in part by the gills. Finally, arterio- or atherosclerosis has not been found in fishes.

Summary

Fishes are susceptible to a variety of parasitic and metabolic diseases, many of which are counterparts of those that occur in mammals. These diseases, together with changes in the physical, chemical and biological characteristics of the environment, are responsible for mortality.

Athero- or arteriosclerosis has not been found in fishes but pathological changes indicative of ageing do occur in other organs. These are cirrhosis and fatty changes in the liver and kidneys, haemochromatosis, hypochromic anaemia, degeneration of mucus-producing glands of the skin, hyperostosis of the haemal arch bones and other vertebral abnormalities.

Some lifespans of fishes in the New York Aquarium and in other institutions are listed. The long-lived fishes kept in captivity have certain general characteristics, and the significance of some of these is discussed.

REFERENCES

BERG, L. S. (1947). Classification of Fishes, both Recent and Fossil. Ann Arbor: J. W. Edwards.
BOURLIÈRE, F. (1946). *Année biol.* **22**, 249.
BREDER, C. M., Jr. (1934). *Zoologica, N.Y.*; **18**, 57.
BREDER, C. M., Jr. (1936*a*). *Bull. N.Y. zool. Soc.*, **39**, 116.
BREDER, C. M., Jr. (1936*b*). *Bull. N.Y. zool. Soc.*, **39**, 149.
BREDER, C. M., Jr. (1952). *Growth*, **16**, 189.
BROWN, M. E. (1957). *In* Physiology of Fishes, **1**, 361. New York: Academic Press.
COMFORT, A. (1956). The Biology of Senescence. New York: Rinehart.
FLOWER, S. S. (1925). *Proc. zool. Soc., Lond.*, 247.
FLOWER, S. S. (1935). *Proc. zool. Soc., Lond.*, 265.
HAFTER, E. (1952). *J. Morph.*, **90**, 55.
HINTON, S. (1959). Personal Communication.

JORDAN, D. S., EVERMANN, B. W., and CLARK, H. W. (1930). *Rep. U.S. Comm. Fish.*, No. 1055, 1.
MELLEN, I. (1919). *Rep. N.Y. zool. Soc.*, No. 23, 101.
MELLEN, I. (1925). *Bull. N.Y. zool. Soc.*, **27**, 61.
NIGRELLI, R. F. (1940). *Zoologica, N.Y.*, **25**, 525.
NIGRELLI, R. F. (1943). *Zoologica, N.Y.*, **28**, 203.
NIGRELLI, R. F. (1952). *Ann. N.Y. Acad. Sci.*, **53**, 1076.
NIGRELLI, R. F. (1954*a*). *Trans. Amer. Fish. Soc.*, **83**, 262.
NIGRELLI, R. F. (1954*b*). *Trans. N.Y. Acad. Sci.*, **16**, 296.
RASQUIN, P., and HAFTER, E. (1951). *J. Morph.*, **89**, 397.
TOWNSEND, C. H. (1904). *Bull. N.Y. zool. Soc.*, No. 14, 163.
TOWNSEND, C. H. (1913). *Bull. N.Y. zool. Soc.*, **16**, 1049.
TOWNSEND, C. H. (1928*a*). *Bull. N.Y. zool. Soc.*, **31**, 11.
TOWNSEND, C. H. (1928*b*). *Rep. U.S. Comm. Fish.*, No. 1045, 249.
WALFORD, L. A. (1958). Living Resources of the Sea., New York: Ronald Press.

DISCUSSION

Rockstein: Which is the longest-lived freshwater fish known?

Nigrelli: In captivity it is this sturgeon which lived 69 years.

Beverton: Sturgeons are also the longest-lived according to field observations; the longest we have ever seen recorded was 151 years, an estimate based on the number of rings in the rays of the pectoral fin. Are any age determinations of the conventional kinds done on these fish at death?

Nigrelli: We have attempted to make age determinations but we have given it up as hopeless because at these steady temperatures they lose the markings. We do take measurements of the fish though, to give us some idea of growth.

Scheidegger: In which organs have you found cancer?

Nigrelli: In practically every organ. We have also seen virus tumours, and I have published a paper (Nigrelli, 1952) on virus in relation to cancer. There are two or three interesting "tumours", however, that are not of the neoplastic type, and one is well known in Europe—it is called lymphocystis disease (Nigrelli, 1954*a*). It was first described in English plaice but it is widely distributed both in freshwater and marine species. This is a hypertrophy of the connective tissue cells in which diseased cells blow up from about 10 μ to 0·5 mm. or more. This disease was definitely shown to be of virus origin.

Holt: Most of the long-lived species are rather large, but there are clear exceptions, just as there are for mammals, where rats and bats of roughly the same size, as Mr. Sacher pointed out, have quite

different lifespans. We find the exceptions among the large fish in that sturgeons and tunas of about the same size have quite different growth rates and lifespans, but I do not know any examples of very small fish which are long-lived. None of those indicated as reaching 20 years or more were small species. By small fish I mean those with low upper limits to L_∞. Are there some such fish which commonly live for ten years or more?

Comfort: There is a reported instance of a goldfish being kept till 40, but it was small and had been kept in a barrel. (Hervey, G. F., and Hems, J. (1948). The Goldfish. London: Batchworth Press.)

Nigrelli: That is an important factor in aquarium management. Fish are restricted in size by the size of the container, though not necessarily by the volume of water. Tarpon have been kept, for instance, for seven or eight years, and some have never grown larger than about 18 inches. An 8-year-old tarpon in the wild might be about 4 feet long or more.

Holt: By small fish, I did not mean fish which were artificially kept small, but ones which cannot grow big no matter how much food or space they are given.

Nigrelli: There are several examples of small fish, like goldfish, that live for about ten years (see Table III).

Comfort: The matter of fatty degeneration is one which has always puzzled me when looking at pathological sections. The normal liver, in the guppy at any rate, looks very fatty but I do not know if it is degenerate. In underfed fish the liver is much more cellular.

Nigrelli: Glycogen infiltration is also evident in stained sections.

Comfort: I suspect that a lot of what appears to be degeneration is reversible, and is actually fat storage.

Nigrelli: We call it fatty change and it does indicate a disturbance of lipid metabolism that is not reversible.

Comfort: I believe you showed that fatty degeneration occurs in small aquarium fish fed only with enchytrae and nothing else?

Nigrelli: That is correct.

Bourlière: It is interesting to notice that tuna are said to have a higher internal temperature than most of the other marine fish of similar size. Maybe there is here again a correlation between metabolic rate, growth rate and ageing rate.

Has any study ever been made on the relative incidence of the various pathological causes of death in wild fish?

Beverton: I do not know of any comprehensive study. A member of the Aberdeen Fisheries Laboratory has taken it up as his special subject in the last year or so.

Nigrelli: No critical work has ever been done to determine the exact meaning of natural mortality. Fishery biologists lump many things under this item. For example, epidemics of myxosporidiosis are quite common but not recognized, and the disease affects young populations much more than the old. Such an infection may be diffuse. All it takes to kill off a population after an epidemic is a slight change in environment, as the fish are already weakened by the disease. These diseases are often self-limiting, and if the fish can survive to, say, a year old, then they apparently can withstand changes in temperature, or other factors including pollution. If the fish die and are not examined for disease the death is then attributed to natural mortality.

Holt: There is a current work which is relevant to this question but it is being done for another reason. Quite intensive population studies of parasitization are being carried out on cod and salmon in an attempt to identify races or sub-populations. The results may well help us to interpret the mortality rates of, say, different sub-populations of the same species.

Bourlière: Are there any indications about the rate of infestation by the various parasites in wild fish? Is it as great as in captive ones?

Gerking: There have been some studies made in Canada of *Triaenophorus* (a tapeworm) infestation in whitefish, because it reduces their market value. There have been attempts made to reduce the incidence of this parasite by eliminating, as much as possible, the intermediate hosts, and there has been partial success.

Rockstein: What is the rate of growth of the common carp, and its longevity? It is a fairly large fish, and it must therefore grow rather rapidly.

Nigrelli: I cannot tell you about that.

Gerking: One of the most recent developments in the study of large fish with rapid growth is some work on the sailfish in Florida waters (de Sylva, D. (1957). *Bull. Mar. Sci. Gulf and Carib.*, 7, 1). It is a well-known sport fish because it is large and can be caught on hook and line. It was amazing to learn that these fish grow very rapidly, living only four or five years, yet reaching 100 lb.

Holt: Carp grow rapidly, but they have a low K; that is, their increments in length tend to be constant, but they have a particularly plastic growth. I think it is one of the few larger species in which there is some evidence of a post-reproductive phase.

Gerking: Is that well documented?

Holt: No—except that I believe in pond culture it is the practice not to keep large carp because their reproductive capacities are beginning to fall off.

Comfort: Goldfish breeders, who are not scientists, say that very often when a goldfish gets to about 16 years of age and is post-reproductive, it improves in condition and size for show purposes, and that a goldfish between the ages of 16 and 20 will often be a very large and particularly glossy specimen for show purposes.

Gerking: What was said about the carp is true of trout also. Breeders do not keep old trout around because they are not efficient reproductively. This is not due to a sterility factor, however, but it reflects the growth of the gonad in relation to the weight of the trout. This is a special case that I did not have time to mention. The growth of the gonad is not proportional to the growth of the fish. Therefore, older trout do not produce as many eggs as a younger one does in proportion to the weight of the fish. It is more efficient for the hatchery to keep younger fish for breeding than it is to keep the same weight of older fish.

Nigrelli: There are many parasites that affect the gonads. If there is an epidemic of gonadal strigeidiasis in any population, it will affect the reproductivity for that particular time.

Holt: Would you suggest, then, that the older fish has had a longer time to be exposed to infestation, and therefore might be more likely to have a low rate of reproduction?

Nigrelli: No, it would have to be an acute infection of some kind, which could spread around by contact, particularly in close schools of fish. Tuberculosis of the ovaries and testes will be found in relatively older fish.

Beverton: You gave us examples of fish living quite happily under extreme environmental conditions. The opposite occurs as well. We have done some work on the Arctic cod over the last few years, and that is an interesting example of a fish which is living on the borderline of its environmental tolerance. When it goes across that border, in effect into the cold water from the Polar basin, the cold water seems to cause quite a substantial mortality. The immediate cause of death seems to be a breakdown in the osmoregulation, and the blood saline of these fish that are caught in cold water is up to four times the normal level. It is difficult to measure mortality in that case, but the inference is that the cold had quite a substantial effect.

Danielli: If fish of the same age are put in different-sized containers, they grow to different sizes. What happens if they are put into a larger container which is separated into two compartments, one large and one small, with a perforated screen which allows the passage of water but not of fish?

Comfort: I have tried this with guppies. If you confine a fish in a

perforated netting cage inside a two-litre jar, it grows at a rate not much less than if it had the full swimming space. I do not think restriction of movement affects the growth of these fish. There is a very different effect when you put more than one fish into a tank. There is a social effect on size, which is partly behavioural and partly chemical. Where the fish have been kept in separate perspex compartments and water comes rapidly through from a large tank, they seem to grow at a not much lower rate than they would have grown if they had been loose in the tank.

Gerking: Many fish are very aggressive to others around them. A fish in company with others will fight or nip in an attempt to maintain territory. The social hierarchy is similar to that which has been described for the chicken and many other animals. These social factors play an important rôle in the rate of growth of fish kept together in aquaria.

Danielli: Has the experiment been tried of taking fish out of a tank in which a "pecking" order has been established, and putting them into a mirrored tank?

Comfort: No, but if you remove the largest fish from a tank in which a size hierarchy has been established, for no good reason everybody "moves up" one place.

Danielli: The fish in the mirrored tank would see one exactly the same size as itself.

Comfort: You might try an enlarging mirror! This should be done with other fish and not with guppies, because guppies are extremely unaggressive. I have been very fortunate in having guppies which have never shown any sign of eating their young, and the counts from trap tanks are no higher than without traps. This is not true of all breeds of guppy, and it would be a perpetual reservation on all this work if the fish fight and eat each other's young.

FACTORS INFLUENCING THE LIFESPAN OF BEES

Anna Maurizio
Bienenabteilung, Liebefeld-Bern

The lifespan of the honey-bee and its dependence on internal and external influences have been the subject of numerous investigations during the last ten years. The problem is a complex one because the honey-bee does not exist as an individual insect but as a member of a colony. The characteristics of the honey-bee must therefore be considered not only from the point of view of the solitary insect, but also from that of the colony. The lifespan of the colony is theoretically unlimited, but that of the individual bee is quite short. The lifespan is also very closely related to the physiological condition of the individual, which in its turn depends on the environment, nutrition and general condition of the colony. The author would therefore like to present this communication in two parts:

(1) the lifespan of the bee in a free-flying colony, and
(2) the lifespan of the bee when separated from the colony and caged.

Lifespan and Physiological Condition of Bees in a Free-Flying Colony

In those regions of the Temperate Zone marked by clearly defined seasons, the colony is inhabited by two types of bees: summer bees and winter bees. These represent two entirely distinct generations of bees with regard to their lifespan, their physiological condition and their mode of life. Here we are confronted with one of the most important and interesting

phenomena in the life of a bee colony, namely, overwintering, or the bridging of an unfavourable season during which the bees cannot forage for food.

More primitive social insects like bumble-bees and wasps solve this problem by dispersing the colony in the autumn, leaving only the inseminated females to overwinter. In the case of the honey-bee, however, the entire colony overwinters with the queen, and the rearing of the first spring brood takes place before the active season begins. The difficulties of overwintering are overcome by producing in the autumn a long-lived generation with big body reserves; the colony is thus enabled to live through the winter and rear the first spring generation.

To understand this, one has to consider in greater detail the characteristic habits of the summer and winter bees, and the ageing and seasonal changes which certain organs undergo. In particular, the pharyngeal glands and the fat body are affected; the wax, mandibular, and salivary glands, and the ovaries of the working bees, are also affected, though to a lesser extent (Anderson, 1931; Armbruster, 1931; El-Deeb, 1952; Evenius, 1937; Farrar, 1936, 1949*b*, 1952; Freudenstein, 1924; Gontarski, 1950, 1954; Haydak, 1934, 1937*a*, *b*, 1939, 1940*a*, *b*; Haydak and Tanquary, 1943; Koehler, 1921; Kratky, 1931; Levin and Haydak, 1951; Lotmar, 1939; Mauermayer, 1954; Maurizio, 1946, 1954; Nickel and Armbruster, 1937, 1938; Phillips, 1922, 1928; Ribbands, 1953; Rockstein, 1950*a*; Zander, 1947, 1951).

Let us begin with the summer bee. In Central Europe it is to be found in the colonies between May and August. Its lifespan varies from a minimum of 25–35 days to a maximum of 60–70 days, and it emerges at the height of full colony development. It will find in the colony large patches of open brood, and very often the number of nurses is scarcely sufficient to feed the young larvae. During the first 10–14 days of its life the young bee consumes a large amount of pollen, thus stimulating full development and functioning of the

pharyngeal glands. The newly emerged bee has undeveloped hyaline pharyngeal glands of irregularly angular shape; its fat body consists of a very delicate transparent cell layer without inclusions. In the approximately ten-day-old summer bee performing nursery duties, the pharyngeal glands are rounded, milky-white to yellow, with well-filled lobes completely covering the secretory ducts. In its third week of life, when the bee assumes different duties, the pharyngeal glands slowly degenerate but the wax glands attain full development. In the four-week-old summer flying-bee the pharyngeal and wax glands have already degenerated, and under normal conditions the fat body of the summer bee remains undeveloped throughout its life. This form of presentation is somewhat schematic, because we know from studies carried out by Lindauer (1953), Ribbands (1952), Sakagami (1953), and others that the division of labour within the colony varies greatly; thus it is possible that the length of any of the above-mentioned duties can be prolonged, shortened or even omitted, and the degree of development of the pharyngeal and wax glands shows parallel fluctuations.

The life of the bee emerging in autumn follows quite a different course. The bee makes its appearance in the colony at a time when the brood is greatly reduced, the stores prepared and the bees ready for overwintering. The young bee feeds for several weeks on pollen without having to perform nursery duties (maximal pollen consumption is between September and October—Lotmar, 1939). Thus the pharyngeal glands and the fat body attain full development and remain in this state until spring, when the autumn bee takes up the nursing of the newly emerging brood. The pharyngeal glands of the winter bee therefore remain in the nursing state for six to seven months, and the fat body consists of several densely folded layers, the cells of which are milky-white, rounded, and packed full with inclusions. At the same time the bee's expectation of life increases, and it becomes a long-lived winter bee, remaining in the colony six to eight months

(maximum expectation of life 300–400 days—Anderson, 1931; Farrar, 1949*a*; Lotmar, 1939; Maurizio, 1954).

Many attempts have been made to explain these striking differences between the lifespan of summer and winter bees. The customary conception is that the lifespan is regulated, in particular, by the collecting activity of the bee outside the hive. According to this conception the bee works itself "to death" on its collecting flights, when death is often caused by accidents (Phillips, 1922, 1928). However, exacting experiments have proved that where death is due to foraging the shortening of life is only a matter of between four and eight days, and thus is not long enough to explain the difference in lifespan between summer and winter bees (El-Deeb, 1952; Mauermayer, 1954). The genetically conditioned differences in lifespan between bees of different races and cultivated strains are also few. The bee is subject—like any other living creature—to the process of physiological ageing, which is based on the destruction of certain nerve cells. Rockstein (1950*a*, *b*, 1953) and Weyer (1931) established that in the ageing bee the number of nerve cells in the olfactory lobe and in the lower pharyngeal ganglion decreases by 35 per cent.

Factors influencing the bees' lifespan become clear only when one considers the behaviour of bees under experimental conditions. For example, if one forces a young summer bee in the nursing state to undertake continuous brood-rearing, the pharyngeal glands will remain at their full development for several weeks and thus increase its lifespan (Moskovljevic, 1939). This increase, as well as an enhancement of physiological condition, accompanies the limitation of brood nests in a colony ready to swarm. Particularly striking is the behaviour of bees when put into a queenless or broodless colony during the summer. Such bees not only possess for several weeks fully developed pharyngeal glands, but also form a winter fat body and thus become long-lived (maximum life-span 166 days, as against 38 days in a colony with brood—Maurizio, 1954). Therefore it is possible to transform a

summer bee during the active season into a physiological winter bee by preventing it from brood-rearing.

Further indications of the interdependent effects of food, care of brood, physiological condition and lifespan were obtained from experiments carried out with bees separated from their colony, and kept in cages or in small experimental colonies.

Lifespan and Physiological Condition of Caged Bees

In the experiments with caged bees attempts were made to clarify the following questions:

(a) What effect has pollen-feeding on caged bees and are there any differences in the effects of pollen from various plant species?

(b) Which organs of the bee depend directly on the food-composition?

(c) Does a direct relationship exist between physiological condition and lifespan?

(d) Which substances in the pollen are decisive in the activation of the physiological condition, and in the lifespan?

The first investigations in this direction go back to the time when Czech workers (Soudek, 1927; Hejtmanek, 1933, 1943; Svoboda, 1940) observed that the pharyngeal glands of newly emerged bees could be brought to full development by feeding with pollen, soya flour and albumin. Subsequently, the present author proved (1946, 1954) that pollen-feeding of caged bees not only brought about an activation of the pharyngeal glands, but also caused a building-up of the fat body, the development of the ovaries, and a statistically proved longer lifespan. These findings were confirmed by other workers (Back, 1956, 1959; Bertholf, 1942; Beutler and Opfinger, 1949; Freudenstein, 1958; de Groot, 1953; Hess, 1942; Müssbichler, 1952; Pain, 1951*a*, *b*; Wahl, 1956), and it was also shown that pollen-feeding produces development of the wax glands (Freudenstein, 1958).

These experiments further confirmed that pollens of different plants can vary greatly in their effect on the bees. Thirty-five pollen samples were examined and these can be divided into many different groups. Depending on their biological effectiveness, they range from the very effective (e.g. *Salix* spp., fruit trees, *Papaver* spp., *Zea mays*, *Crocus albiflorus*, *Trifolium* spp., *Castanea sativa*) to the almost ineffective, e.g. all seven species of conifer examined (*Pinus cembra*, *P. silvestris*, *P. montana*, *Picea excelsa*, *Abies alba*, *Cedrus libani*, *Pseudotsuga taxifolia*). No relationship could be established between the type of floral biology of any particular plant and the effectiveness of its pollen on bees; on the other hand, pollen collected by bees was more effective than hand-collected pollen from the same plant species. It remains to be mentioned that bees are very selective in their choice of pollen sources, and this, according to Louveaux (1958), is connected with the nitrogen content of the pollen. These observations on bees were recently confirmed by experiments carried out with other insects (*Tribolium* larvae, Koch, 1952; *Osmia lignaria*, Levin and Haydak, 1958). These authors also established differences in effectiveness between pollen from different plant species and between hand and insect-collected pollen.

Further evidence shows that the effect of pollen is time-conditioned, i.e. consumption must take place within the first 10–14 days of the bee's life in order to activate the pharyngeal and wax glands as well as the fat body. Pollen-feeding at a later stage has little or no effect (Beutler and Opfinger, 1949; Freudenstein, 1958; de Groot, 1953; Kratky, 1931; Maurizio, 1954).

Data obtained from the author's experiments were statistically interpreted in order to examine in greater detail the relationship between lifespan and physiological condition. On the basis of a multiple correlation (part-regression) it was established that there is a positive relationship between physiological condition and lifespan, i.e. that 56 per cent of

the variations in lifespan can be traced to the physiological condition. The closest correlation was found between the development of the fat body and lifespan; the least close was that between ovary development and lifespan. The result of this statistical evaluation confirmed the biological investigations which showed that the main function of the fat body is the storing of protein, glycogen and fat, whereas the pharyngeal glands not only serve as a store, but perform other important functions such as the secretion of larva food and the enzymes necessary for honey production. The functioning of the ovaries of the workers is mainly controlled by hormones and in the queenright colony the ovaries remain undeveloped (Butler, 1954, 1955, 1956; Pain, 1954, 1958; and Voogd, 1955). Thus, of all the organs examined, it appears that the fat body plays the most important rôle in the regulation of lifespan of the summer and winter bee.

A further problem is posed in deciding which substances in the pollen are responsible for the activation of the physiological condition and lengthening of the bees' lifespan. Pollen is rich in carbohydrates, fats, proteins, vitamins and minerals, but the concentration of any one of these substances varies greatly from one plant species to another (Haydak and Palmer, 1938, 1940, 1941, 1942; Haydak and Vivino, 1943, 1950; Hejtmanek, 1943; John, 1958; Kocher, 1942; Pearson, 1942; Sarkar *et al.*, 1949; Todd and Bretherick, 1942; Vivino and Palmer, 1944; Weaver and Kuiken, 1951; Weygand and Hofmann, 1950). For instance, the protein content of different types of pollen can vary as much as 5 to 35 per cent, and the spectra of amino acids present may be variously composed. It was found that pollen contains the following vitamins: B_1 (thiamine), B_2 (riboflavin), B_6 (pyridoxine), nicotinic acid and biotin. Moreover vitamin K, which is not normally present in fresh pollen, was found in pollen obtained from comb cells. Bees have sufficient carbohydrates at their disposal in honey, thus pollen is their main protein and vitamin source. Over the last few years many lively discussions

have taken place on the relationship between lifespan and physiological condition in the adult bee, and to what extent it is influenced by the proteins and vitamins of pollen. It must be pointed out that this concerns only the vitamin requirements of the adult bee, as there are no doubts about the vitamin requirements of the brood.

The results of the experiments carried out so far can be summarized as follows (Back, 1956, 1959; Freudenstein, 1958; de Groot, 1953; Haydak and Vivino, 1950, Koch and Schwarz, 1956; Maurizio, 1954; Müssbichler, 1952; Pain, 1951*a*, *b*). In the caged young bee lifespan and physiological condition are closely related to the protein content of food. Bees fed exclusively on devitaminized casein develop pharyngeal glands, fat bodies and ovaries, and a statistically proved increase of lifespan is observed by comparison with bees of the same age fed on a pure sugar diet. An increase in nitrogen and in dry weight occurs in the young bee if it is fed from its emergence onwards on synthetic food—a mixture of sugar and pure amino acids (de Groot, 1953). Addition of any one of the vitamins (B_1, B_2, B_6, nictotinic and pantothenic acids) resulted in no statistically proved increase in lifespan, but addition of vitamins to a protein-containing diet influenced the development of the pharyngeal and wax glands. Although young bees can develop their pharyngeal glands on vitamin-free casein food, the degree of development is enhanced if vitamins are added. Back's latest investigations contribute greatly towards a solution of this question. According to her, large doses of vitamins added to the casein food have the effect of shortening the lifespan. A very slight prolongation was observed when very weak mixtures of vitamins were added (mixture: B_1, B_2, B_6, A, C, E, K, nicotinic, pantothenic and folic acids, biotin and inosite). Young bees fed with vitamin-free casein food reared one generation of normal brood; bad rearing occurred only with the second generation of larvae. Young bees reared by nurses fed on a vitamin-free diet are unable to utilize the protein in their food and thus

cannot rear a brood unless vitamins are added to their diet. In such vitamin-starved bees addition of pantothenic acid or a mixture of vitamins to the diet will restore normal brood-rearing within 24 hours.

Apparently the newly emerged young bee is left with large body reserves of vitamins, thus making it possible to develop its pharyngeal glands, lengthen its lifespan and rear one brood-generation in spite of consuming a protein-rich but vitamin-free diet. It seems, however, that this vitamin reserve is not sufficient to pass on to the brood an adequate vitamin surplus; so that the second generation of vitamin-starved bees shows signs of vitamin deficiency, i.e. the development of the pharyngeal glands and the lifespan are affected. Similarly, a colony of bees kept on a protein-free diet are able to raise one generation of normal brood by using up their own protein reserves (Haydak, 1935).

Discussion

Present-day knowledge of the inter-effects of nutrition, physiological condition and lifespan of the bee, and of the processes of life in the colony throughout the year, can be summarized as follows:

(1) Pollen is the main source for protein, vitamins, and minerals, and therefore forms, with the sugar-containing juices, the basis of nutriment and development of the bee colony. Pollen-feeding of the young bee promotes the development of the pharyngeal and wax glands, the formation of a many-layered fat body and an increase in lifespan. Of all the pollen substances proteins are the most decisive in influencing the lifespan and physiological condition of the bee. For the adult bee vitamins in food are less essential as it still has a large store of vitamins from the larval phase. Absolutely essential is the extra vitamin supply at the time of brood-rearing. There is a statistically comprehensible correlation between physiological condition and lifespan.

(2) The yearly cycle of life in the bee colony may be

described as follows. During the warm season the young bee feeds for the first few days of its life on pollen, developing its pharyngeal glands. With the commencement of brood-rearing the reserves are used up and the bee ages physiologically, thus becoming a short-lived summer flying-bee. However, if for any cause brood-rearing is limited (e.g. due to a queenless colony, swarming, prolonged rain, etc.), or completely omitted, the pharyngeal glands will remain fully developed, the fat body will be formed and the lifespan thus increased. In the free-flying colony during the active season it is possible to produce experimentally such a generation of physiologically young, long-lived bees.

When brood-rearing is naturally limited and at the same time intensive pollen-feeding takes place, a long-lived winter bee with large body reserves, fully developed pharyngeal glands and a many-layered fat body is produced in late summer or autumn; the bee is thus enabled to overwinter and to rear the first brood in spring. During the winter the bee feeds almost entirely on sugar and therefore it seems that the substances (protein, glycogen and vitamins) necessary to survive winter are drawn from the reserves built up in the fat body. A similar kind of overwintering is known of other solitary insects such as *Anopheles*, *Culex*, *Lasiopticus*, *Epistrophe*, *Ips typographus*, etc. (Buxton, 1935; Kuhn, 1949; Schneider, 1947, 1948; Wigglesworth, 1950).

(3) It appears that the lifespan and physiological condition of bees in free-flying colonies depend greatly on nutrition and brood-rearing. Long-lived bees always appear in a colony where a rich supply of pollen is available and where little or no brood is in need of nursing. In our climate long-lived bees appear in autumn and winter, but under different climatic conditions this may occur at different times or fail to take place. Thus the physiological condition of the "summer" and "winter" bee does not depend on a certain season, but can be promoted at any time as a reaction to external conditions essential to life.

The continuity of life in a bee colony depends upon an unbroken succession of generations. This succession is maintained by the fluctuations between nutrition, brood-rearing, physiological condition and lifespan, giving the colony adaptability to the prevailing external conditions.

The greater the brood nest is in proportion to the number of nursing bees, the larger is the new batch of young bees, but the shorter the lifespan of the individual insect. Restricted brood areas resulting in small numbers of young bees, on the other hand, mean long-lived bees. Both types of colony are well known to the practising bee-keeper. These types are partly genetically conditioned, it being probably less the longevity of the bees which is hereditary than the tendency to the laying down of large or small brood nests.

[The editors would like to thank Mrs. M. Silverman for her work in translating this paper, and Mr. H. K. Airy Shaw for his expert advice.]

REFERENCES

ANDERSON, J. (1931). *Bee World*, **12**, 25.
ARMBRUSTER, L. (1931). *Handb. Ernähr. Nutztiere*, **3**, 478.
BACK, E. (1956). *Insect. Soc.*, **3**, 285.
BACK, E. (1959). Personal communication.
BERTHOLF, L. M. (1942). *J. econ. Ent.*, **35**, 887.
BEUTLER, R., and OPFINGER, E. (1949). *Z. vergl. Physiol.*, **32**, 383.
BUTLER, C. G. (1954). *Bee World*, **35**, 169.
BUTLER, C. G. (1955). *Amer. Bee J.*, **95**, 275.
BUTLER, C. G. (1956). *Proc. roy. Soc., A.*, **31**, 12.
BUXTON, P. A. (1935). *Parasitology*, **27**, 263.
EL-DEEB, A. L. A. (1952). *Amer. Bee J.*, **92**, 517.
EVENIUS, C. (1937). *D. Imkerführer*, **11**, 128.
FARRAR, C. L. (1936). *Amer. Bee J.*, **76**, 452.
FARRAR, C. L. (1949*a*). *Bee World*, **30**, 51.
FARRAR, C. L. (1949*b*). *In* The Hive and the Honeybee, ed. Grout, R.A. Hamilton, Illinois: Dadant.
FARRAR, C. L. (1952). *J. econ. Ent.*, **45**, 445.
FREUDENSTEIN, K. (1924). *Arch. Bienenk.*, **6**, 49.
FREUDENSTEIN, H. (1958). In *XVII Congr. int. Apic.*
GONTARSKI, H. (1950). *Imkerfreund*, **11**, 183.
GONTARSKI, H. (1954). *Z. Bienenforsch.*, **2**, 161.
GROOT, A. P. DE (1953). Dissertation, Utrecht.
HAYDAK, M. H. (1934). *J. agric. Res.*, **49**, 21.

HAYDAK, M. H. (1935). *J. econ. Ent.*, **28**, 657.
HAYDAK, M. H. (1937*a*). *J. agric. Res.*, **54**, 791.
HAYDAK, M. H. (1937*b*). *Ann. ent. Soc. Amer.*, **30**, 258.
HAYDAK, M. H. (1939). *J. econ. Ent.*, **32**, 663.
HAYDAK, M. H. (1940*a*). *J. econ. Ent.*, **33**, 397.
HAYDAK, M. H. (1940*b*). *Glean. Bee Cult.*, **68**, 615.
HAYDAK, M. H., and PALMER, L. S. (1938). *J. econ. Ent.*, **31**, 576.
HAYDAK, M. H., and PALMER, L. S. (1940). *J. econ. Ent.*, **33**, 396.
HAYDAK, M. H., and PALMER, L. S. (1941). *J. econ. Ent.*, **34**, 37.
HAYDAK, M. H., and PALMER, L. S. (1942). *J. econ. Ent.*, **35**, 319.
HAYDAK, M. H., and TANQUARY, M. C. (1943). *Bull. Minn. agric. Exp. Sta.*, **160**, 1.
HAYDAK, M. H., and VIVINO, E. (1943). *Arch. Biochem.*, **2**, 201.
HAYDAK, M. H., and VIVINO, E. (1950). *Ann. ent. Soc. Amer.*, **43**, 361.
HEJTMANEK, J. (1933). *Čes. Včelař*, **10**.
HEJTMANEK, J. (1943). Die Pollenverdauung der Honigbiene, Ustr. slov. vcel. spolkov, Prievidza.
HESS, G. (1942). *Beih. Schweiz. Bienenztg.*, **1**, 33.
JOHN, M. (1958). *Z. vergl. Physiol.*, **41**, 204.
KOCH, A. (1952). *Tijdschr. Ent.*, **95**, 166.
KOCH, A., and SCHWARZ, J. (1956). *Insect. Soc.*, **3**, 213.
KOCHER, V. (1942). *Beih. Schweiz. Bienenztg.*, **1**, 155.
KOEHLER, A. (1921). *Schweiz. Bienenztg.*, **57**, 424.
KRATKY, E. (1931). *Z. wiss. Zool.*, **139**, 120.
KUHN, W. (1949). *Mitt. Schweiz. ZentAnst. Forstl. Versuchsw.*, **26**, 245.
LEVIN, M. D., and HAYDAK, M. H. (1951). *J. econ. Ent.*, **44**, 54.
LEVIN, M. D., and HAYDAK, M. H. (1958). *X Int. Congr. Ent.*, **4**, 1079.
LINDAUER, M. (1953). *Bee World*, **34**, 63, 85.
LOTMAR, R. (1939). *Landw. Jb. Schweiz.*, **53**, 34.
LOUVEAUX, J. (1958). Thèse, Paris.
MAUERMAYER, G. (1954). *Arch. Bienenk.*, **31**, 31.
MAURIZIO, A. (1946). *Beih. Schweiz. Bienenztg.*, **2**, 1.
MAURIZIO, A. (1954). *Landw. Jb. Schweiz.*, **68**, 115.
MOSKOVLJEVIC, V. (1939). *Schweiz. Bienenztg.*, **75**, 689, and *Bee World*, **21**, 39.
MÜSSBICHLER, A. (1952). *Z. vergl. Physiol.*, **34**, 207.
NICKEL, H. K., and ARMBRUSTER, L. (1937). *Arch. Bienenk.*, **18**, 257.
NICKEL, H. K., and ARMBRUSTER, L. (1938). *Arch. Bienenk.*, **19**, 134.
PAIN, J. (1951*a*). *Arch. int. Physiol.*, **59**, 203.
PAIN, J. (1951*b*). *C. R. Soc. Biol.* (*Paris*), **165**, 1505.
PAIN, J. (1954). *Insect. Soc.*, **1**, 59.
PAIN, J. (1958). *Apiculteur*, **103**, 1.
PEARSON, P. B. (1942). *Proc. Soc. exp. Biol.* (*N.Y.*), **51**, 291.
PHILLIPS, E. F. (1922). *J. econ. Ent.*, **15**, 368.
PHILLIPS, E. F. (1928). Beekeeping. New York: Macmillan Co.
RIBBANDS, C. R. (1952). *Proc. roy. Soc. B.*, **140**, 32.
RIBBANDS, C. R. (1953). The Behaviour and Social Life of Honeybees. London: Bee Research Association Ltd.

Rockstein, M. (1950*a*). *Ann. ent. Soc. Amer.*, **43**, 152.
Rockstein, M. (1950*b*). *J. cell comp. Physiol.*, **35**, 11.
Rockstein, M. (1953). *Biol. Bull., Wood's Hole*, **105**, 154.
Rösch, G. A. (1925). *Z. vergl. Physiol.*, **2**, 571.
Sakagami, S. F. (1953). *Jap. J. Zool.*, **11**, 117.
Sarkar, B. C. R., Wittwer, S. H., Luecke, R. W., and Shell, H. M. (1949). *Arch. Biochem.*, **22**, 352.
Schneider, F. (1947). *Mitt. schweiz. ent. Ges.*, **20**, 306.
Schneider, F. (1948). *Mitt. schweiz. ent. Ges.*, **21**, 249.
Soudek, S. (1927). *Bull. Fac. Agric. Brunn*, **10**, 1.
Svoboda, J. (1940). *Schweiz. Bienenztg.*, **76**, 206.
Todd, F. E., and Bretherick, O. (1942). *J. econ. Ent.*, **35**, 129.
Vivino, E., and Palmer, L. S. (1944). *Arch. Biochem.*, **4**, 129.
Voogd, S. (1955). *Experientia*, **40**, 181.
Wahl, O. (1956). *Südwestdtsch. Imker*, **8**, 348.
Weaver, N., and Kuiken, A. (1951). *J. econ. Ent.*, **44**, 635.
Weyer, F. (1931). *Z. Zellforsch.*, **14**, 1.
Weygand, F., and Hofmann, H. (1950). *Chem. Ber.*, **83**, 405.
Wigglesworth, V. B. (1950). The Principles of Insect Physiology, 4th ed. London: Methuen.
Zander, E. (1947). Das Leben der Biene, 5th ed. Stuttgart: Ulmer.
Zander, E. (1951). Der Bau der Biene, 4th ed. Stuttgart: Ulmer.

DISCUSSION

Wigglesworth: Have you considered the further complication that building up of these reserves may not be a direct effect of the various nutrients, but an effect through the endocrine system? For example, it has long been known that in many adult insects deprived of the corpus allatum the eggs do not develop and do not build up yolk. There is the same effect in protein starvation, where the same histological effects appear. A. S. Johansson (1958. *Nature* (*Lond.*), **181**, 198), working on the milkweed bug, showed that if an active corpus allatum is implanted in the starved insect there is normal egg development. In other words, the immediate effect of protein feeding seems to be to activate the corpus allatum. The prime deficiency in a protein-starved insect is inactivity of the gland. In your experiments it would not necessarily be the corpus allatum; it might be the neurosecretory cells or some other component in the endocrine system.

Hinton: In bees doesn't the queen substance inhibit the development of the corpora allata and keep their volume small?

Maurizio: The degree of development of the ovaries of the honeybee worker is directly connected with the endocrine system and the queen substance (see references to Butler, Pain and Voogd). It is

possible that the development of the pharyngeal glands and the fat body also come under endocrine influence but, as far as I know, this has not yet been examined closely in the honey-bee.

Rockstein: Dr. Maurizio did imply in her paper that it was a matter of endocrine control. I personally think that, generally, the ultimate controlling influence will be found to lie in the endocrine system. I do not think that Dr. Maurizio said that vitamins or proteins were involved in this physiological senescence. She did indicate that there was a depressed development of the pharyngeal gland, which suggests hormone control.

Comfort: Is the rate of loss of nerve cells different in summer and winter bees?

Rockstein: At the two levels of the brain which were counted there were about 500 cells in the young bees and only about 325 in the old bees, regardless of whether these were indoor (summer) bees without a queen, or outdoor (summer) bees which had been living a normal life in the hive.

Comfort: In other words the difference in lifespan does not depend on the difference in the rate of loss of cells?

Rockstein: Yes, it does, because the old bees in both conditions showed precisely the same degree of loss. The outdoor bees I had were only seven weeks old, whereas, indoors, I had bees still living at ten weeks of age. For one thing, my bees were exposed to light 24 hours a day. According to Dr. Maurizio the activity may have nothing to do with age, but nevertheless I could not keep them alive any longer under these conditions even on a completely unlimited diet. I do think that the similarity in development of the overwintering or the summer-broodless bees is very significant. It points to an entirely different phenomenon from that in the caged bees—namely that these summer, "queenright" animals normally are not able to attain their potential longevity owing to the demands of brood-rearing upon their nutrition. As soon as you eliminate this really exorbitant nutritional demand, by removing the queen, the bees are able to attain a lifespan of something like six to eight months. As Prof. Wigglesworth suggested and Dr. Maurizio implied, the diet does this, but where it produces its primary effect is not known. Most probably it is through the endocrine system; certainly, that is evident in the effect upon the development of the pharyngeal glands and of the fat body, which must be controlled at a biochemical level. The most plausible explanation at a biochemical level is that of altering hormone control.

Nigrelli: What would happen if you did not feed the caged bees?

Maurizio: They would be dead of starvation in two or three days.

Nigrelli: Have they no capacity for food storage?

Maurizio: They have proteins but no sugar.

Wigglesworth: As I understand it, the queenless worker develops ovaries but the winter bee does not. That would suggest that there is a more subtle difference in addition to the direct nutritional effect.

Maurizio: The queen substance is there in the overwintering colony.

Wigglesowrth: So there is a dual effect.

Hinton: Do the workers develop ovaries whatever time of the year you remove the queen?

Maurizio: Yes.

Kershaw: There is evidence in blood-sucking flies that they take blood under hormonal influence, and that there is an antibiting hormone (Lavoipierre, M. M. J. (1958). *Nature* (*Lond.*), **182**, 1567). This may be a similar phenomenon.

Maurizio: We will probably ask Dr. Butler to do this experiment with the queen substance.

Bourlière: Have you made any determination of oxygen consumption in winter bees as compared with summer bees?

Maurizio: That was done by Corkins and Gilbert (Corkins, C. L. and Gilbert, C. S. (1932). *Bull. Wyo. agric. Exp. Sta.*, No. 187, 1). They found that carbon dioxide output at a hive temperature of 4° was 52–62 per cent of the output at 16°.

Sacher: Is the difference between summer bees and the overwintering bees in the colony determined directly by nutrition and activity, or is there a change in the behaviour of the colony which is caused by the environment and which in turn leads to these differences?

Maurizio: The winter bees are inactive; there is no brood, they cannot fly and they stay in the colony in a cluster. The only function is to keep warm in the cluster.

Sacher: Then the fact that it gets cold and they cluster in this fashion and cease their brood rearing is what leads to this change in survival.

Maurizio: But the bees begin to brood in February in Switzerland. It depends on the climatic conditions.

Hinton: There must be some indirect effects here because there are many long periods in the winter which are just as warm.

Maurizio: In Northern Europe bees are unable to forage for four or five months in winter, and the brood-interval is much longer than in England and Central Europe.

Rockstein: There may, however, very well be a light-dependent factor, such as a diurnal or photoperiod effect. Thirty minutes

before sundown, for example, most foraging bees will start to come back to the hive, even on a hot summer day, so it is not a matter of temperature.

Holt: What is the mode of life of tropical bees?

Maurizio: I think that in the tropics there are no winter bees, because they can fly all the year. They have pollen and nectar, they seem to have brood the whole year and there are no long-lived bees in the colony. But a proper study of bees in the tropics has yet to be made.

Hinton: That would be primarily an adjustment to food supplies and not necessarily to temperature.

Maurizio: It is complex. In the tropics there may be no overwintering, but during the two or three months of the dry season there may be long-lived bees in the colony.

Rockstein: There is probably more than one factor, such as light or temperature, that would produce the end-result of conserving the colony. In Minnesota, bees begin brood-rearing in January when temperatures are sometimes at −30° F. These animals are being continually decimated during the winter months because some of them have emerged in August, some in September and some in October, and we are going to end up with a very small nucleus from the last-laid eggs by the end of winter. There appears then to be a social pressure upon the hive which stimulates brood-rearing late in the winter. Somehow, the queen is aware of this, even in the dead of winter. As far as light is concerned, the shortest day is in mid-January in Minnesota, but the queen begins to lay eggs again at that time.

Hinton: What is the temperature in the cluster in winter in Minnesota?

Rockstein: The centre of the cluster is always maintained at a temperature of about 33° C. This has been established by thermocouple measurements. The bees on the outside of the cluster change places with bees from the inside; otherwise those on the outside would fall torpid from cold. These outside bees must feed, generate heat, enter and allow the inner bees to move out. If the cluster gets too far away from the food stores, the whole cluster will die, with the queen the last one to go.

Hinton: Thus social insects can be said to be homoiothermic.

Rockstein: I would rather say that the colony as a whole can be said to be homoiothermic.

THE BIOLOGY OF AGEING IN INSECTS

Morris Rockstein

Department of Physiology, New York University College of Medicine, New York

For well over a decade the present author's interest in ageing has been that of establishing firm, quantitative biochemical criteria for physiological ageing, particularly in structures manifesting senescence in the form of declining function as well as degenerative anatomical alterations with advancing age. As a direct consequence of these physiological studies, longevity data have been obtained for large numbers of individuals for each of two species of insects and for strains of similar genetic constitution in each case. This discussion will present details of the lifespan of the common housefly, *Musca domestica* L., and the honey-bee, *Apis mellifera* L., with special emphasis upon recent studies directly concerned with the factors affecting the lifespan of male and female houseflies.

In an earlier series of experiments, involving a comparison of change in cell number with alteration in cholinesterase activity with age, in the adult worker honey-bee (Rockstein, 1950*a*), the time of final samplings of living animals was determined by the availability of sufficient numbers of bees for enzymological and histological evaluation. In all cases this occurred when one per cent or less of the original number of bees employed were still living, and represented values very close to the maximum lifespan for this strain of Italian golden honey-bees. Thus, for 3,750 queenless worker bees, maintained indoors in large cages supplied with honey, pollen and water in excess and exposed to artificial lighting day and night, the final sampling was made at 68 days. A similar value of ten

weeks was obtained for approximately 4,000 of the same strain of honey-bee maintained indoors, in a more recent study involving changes in alkaline and acid phosphatase in ageing bees (Rockstein, 1953). For a similar study of 2,700 "queen-right" bees, marked with coloured lacquer immediately after emergence and returned to the hive to engage in normal hive activities (during the summer months), the last sample of bees had to be taken at 51 days of age. These values compare well with observations of apiculturists and other students of the biology of the honey-bee (see Rockstein, 1950*b*). Indeed, Dr. Maurizio's own studies (1954) include data for two strains of Italian bees of maximum lifespans of 54 and 62 days, respectively, maintained in the hive during summer months.

In the earlier studies (Rockstein, 1950*a*), the number of neurones at two distinct levels of the honey-bee brain was employed as an anatomical criterion for biological old age; the absolute number of cells remaining in the brains of old bees (as well as the percentage loss from emergence to old age) was remarkably similar (325 ; 350) for both kinds of old bees, whether they were living the normal lives of the hive bee or were maintained indoors in a small queenless colony under the conditions described. This loss of about 35 per cent of the original number of brain cells in the adult worker bee is singularly similar to that of a 35 to 40 per cent loss in mammalian brain cell number reported for humans by Hodge (1894), Ellis (1919, 1920), Andrew (1938) and Gardner (1940) and for the white rat by Hatai (1902) and by Inukai (1928).

From a recent study of the decline with age in the activity of enzymes concerned with the energizing of flight activity in the common housefly, from emergence to senility, longevity data have been obtained for thousands of male and female flies of the NAIDM standard laboratory strain of houseflies, which had been intensively inbred for more than one hundred generations. In our laboratory these animals are reared and maintained on a standardized laboratory diet in an air-conditioned room kept at 80° F and 45 per cent relative

humidity. Except for specific experiments designed to test the rôle of parental age in determining the longevity of the offspring, all flies were reared from eggs laid by parents as soon as they were capable of oviposition, i.e. between the fourth and fifth days of adult age. A well-regimented strain under the conditions of rearing and maintenance described, these flies emerge as adults exactly two weeks following the emergence of adults of the previous generation and young females begin laying eggs on exactly the fourth day after they have reached the imaginal state.

Longevity and diet

During the course of collecting adult male and female houseflies for biochemical study (Rockstein, 1956), it was observed that there were relatively fewer and fewer males available for enzyme determinations, especially by the end of the second week. Thus, from a sex ratio of one to one, the male to female population composition fell to a one to two ratio by the end of two weeks and to a less than one to three ratio by the end of the third week. A pilot follow-up study was made of six cages of about 125 flies each in which mortality (rather than survival) counts were made; the results (Rockstein, 1957) clearly confirmed the fact that male longevity was considerably smaller than that of the female housefly. However, in both of these cases, although the larvae were reared on a standard laboratory medium of powdered whole bovine milk (KLIM, Borden's) dried brewer's yeast and agar, the adults had been maintained on sucrose and water alone (in order to eliminate extraneous factors of diet and egg-production in the females particularly, in the age-dependent enzyme study). Under such conditions of restricted diet, it was thought that the observed sex-related differential in longevity, favouring the female of this species, might have resulted from the possible availability of nutrient reserves (such as oöcytes or fully developed ova in the ovarioles of the young female at emergence) to individuals of that sex exclusively. Figs. 1*a* and 1*b*

graphically illustrate the data obtained for two sets of experiments involving a total of 600 males and 600 females maintained as adults on sucrose and water, as before, and 600 males and 600 females maintained on a diet of sucrose, water and powdered whole milk. (The latter is the *normal* diet for stock breeding adult houseflies.) As is clearly seen in Fig. 1*a*,

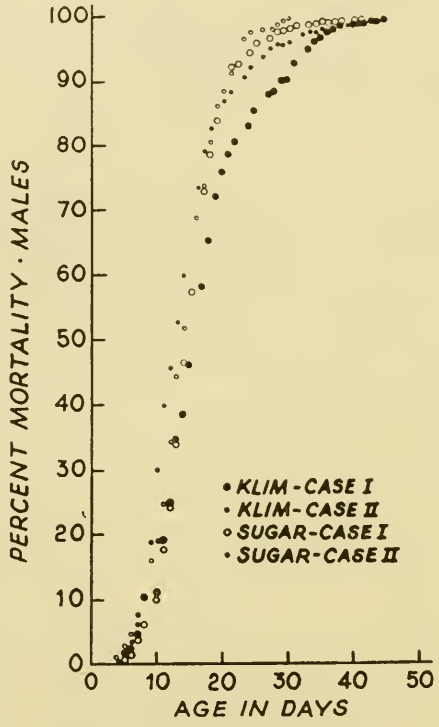


FIG. 1*a*. The effect of diet on male houseflies.

Reprinted from Rockstein and Lieberman (1959), by courtesy the Editor, *Gerontologia*.

no appreciable advantages accrued to the longevity of the male houseflies from inclusion of this (high protein, lactose, butter-fat and mineral-containing) adult dietary component. On the other hand, female flies, with a greater longevity than males even under conditions of restricted diet (sucrose and water alone), showed a considerable prolongation of lifespan as a result of including KLIM in the adult food, beginning with

the second week of life (Fig. 1*b*). As can be seen from Table I (reprinted from Rockstein, 1957), the mean longevity for a total of 600 female flies maintained on the enriched diet was about 31 days, in contrast to a mean value of about 19·5 days for females maintained on sugar and water alone. Moreover, the maximum longevity for females on the KLIM-enriched

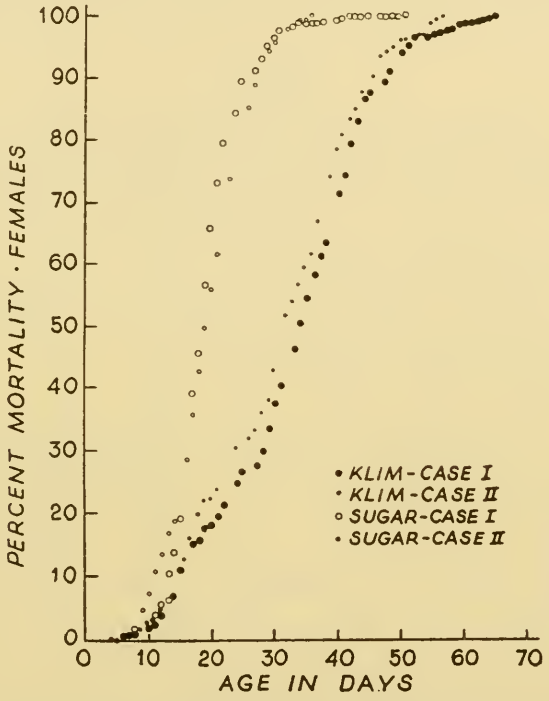


FIG. 1*b*. The effect of diet on female houseflies.

Reprinted from Rockstein and Lieberman (1959), by courtesy the Editor, *Gerontologia*.

diet was about 30 per cent higher than for females on the restricted diet.

These results are in direct contrast to the well-known findings of McCay and his co-workers (1935, 1939, 1941) that *restricting the dietary intake* immediately or soon after weaning retarded the growth of male rats and concomitantly *extended* the average lifespan from 483 to 894 days (and maximum

longevities from 927 to 1,306 days). Female longevities, on the contrary, were relatively unaffected by such alterations in diet. It would appear from their results that retardation of growth in the male rat by such a dietary restriction eliminates the sex differential in longevity, normally favouring the female rat. However, McCay emphasized the *low calorie* aspect of his restricted diet, which was in reality a high protein, salt and vitamin diet. It is therefore likely that the

Table I

EFFECT OF DIET ON LONGEVITY OF MALE AND FEMALE HOUSE FLIES

	With KLIM		*Sugar and water only*		*With KLIM*		*Sugar and water only*	
	Males	*Females*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*
Average longevity (days)	17·5	32·7	15·6	19·5	14·4	30·8	14·6	19·7
Maximum longevity (days)	44	64	40	50	40	56	29	35

critical factor involved in such a restricted diet might well have been the *effective* protein content of the diet. Indeed, the ingestion of such a "low calorie" diet might mean the utilization of the protein in this diet to meet the basal energy requirements (in the absence of carbohydrates and fats customarily utilized by the body in energizing processes). There would result an unavailability of protein required for normal cell growth, replacement and addition and, therefore, retardation of normal body growth and maturation. This (and evidence to follow) suggests that there may exist for each species a specific protein-calorie optimum for normal growth

and maturation. Indeed, an early paper by McCay and Crowell (1934) reported that *reduction in the protein content* of the diet fed to trout doubled their longevity.

In insects too, there appears to be an optimal dietary level of protein for growth and development and indirectly for lifespan. Thus in three species of cockroaches (all of which are *not* fully grown or mature at the onset of the final adult stage), Haydak (1953) reported specific optimum dietary protein requirements both for development and survival of

Table II

EFFECT OF DIET ON THE DEVELOPMENT AND LONGEVITY OF THREE SPECIES OF COCKROACHES (AFTER HAYDAK, 1953)

Effect of diet upon:	*Optimum protein content of diet*		
	P. americana	*B. orientalis*	*B. germanica*
Minimal nymphal mortality: Shortest development period	49%–79%	22%–24%	22%–24%
Greatest average adult longevity	22%	11%	11%

the nymphal instars as well as for longevity of the adult. Table II, prepared from Haydak's data, shows that for the American cockroach the optimum protein for shortest nymphal development and associated lowest nymphal mortality was a broad range of 49–79 per cent; for either the Oriental or German cockroach, this was a much lower 22–24 per cent. For maximum adult longevity, on the other hand, the optimum protein content of the diet was 22–24 per cent for the adult diet of the American cockroach and 11 per cent for both the Oriental and German cockroaches. Haydak concluded from his data that for adults the heaviest protein

eaters had the shortest lifespans and that the *total lifespan* was inversely proportional to the protein intake from eclosion to death.

Maurizio's work has also demonstrated the importance of protein (and possibly vitamins) in the longevity of adult worker honey-bees (1954). She has shown that captive worker honey-bees which are fed pollen early in their adulthood resemble overwintering bees in two major respects; they are longer-lived than similar bees rearing brood and, secondly, their "physiological state", i.e. well-developed fat body and pharyngeal glands maintained for a longer time, is typical of overwintering bees (which may live as long as six to eight months in contrast to six to eight *weeks* for maximum summertime longevities). Thus, retardation of ageing in the worker bee is associated with adequate pollen (protein and vitamin) intake at an early adult age, in the face of reduced demands upon such food reserves, such as occurs in overwintering or non-brooding "summer bees". This in turn results in slow build-up and extended maintenance of those structures upon which the prolongation of adult life is significantly dependent.

In all the cases mentioned above it appears that, where growth or maturation has not yet been completed, an optimum level of food (perhaps protein, specifically) intake is necessary to complete that development. Restricting the diet, as in the case of the young male white rat, trout and at least three species of cockroaches, delays the attainment of adult form and concomitantly defers the cessation of growth and therefore senescence. In the case of holometabolous insects, like the housefly or the honey-bee, the situation is quite different. These animals are essentially fully matured within a few hours to several days, respectively. Heavy demands upon the food (protein) reserves of the female such as oviposition in the case of the housefly (Rockstein, 1958) and brood-rearing in the case of the worker bee *shortens the lifespan* in these animals. One can perhaps speak of a "negative protein

balance" operating against the attainment of the longevity potential of a particular sex for a particular species, when the diet is inadequate for the physiological needs of such animals. Rockstein (1958) suggested that food reserve in the ovaries might indeed be a factor important in higher female longevity even during starvation. In this connexion, a paper by Grosch (1950) has shown that starving female wasps, *Habrobracon juglandis* (Ashmead), draw upon the reserves of the ovarioles, as evidenced by the gradual resorption of ova from the ovarioles which is especially marked during the latter days of their lives. Woke, Ally and Rosenberger (1956) further support this idea of the ovaries as a source of nutrition in starvation for the female mosquito, *Aedes aegypti* L., in the observations that delaying the first blood meal or decreasing the size thereof lowers total egg production markedly. In the Levant housefly, *Musca vicina* Macq., Ascher and Levinson (1956) have also found protein essential to the adult diet for oviposition and cited similar evidence for other species of muscoid adults. However, the common housefly does lay eggs, albeit much more spottily, even on a protein-free diet, but no information is available as to the number and viability of such eggs.

Longevity differences and sex

In order to obtain further insight into the differences between male and female longevities in the housefly, a study on a much larger scale was undertaken. Fig. 2 (taken from Rockstein and Lieberman, 1958) shows the survival curves for about 8,500 flies of both sexes of the same NAIDM strain extending over nine generations, *reared and maintained on a complete diet* under the controlled laboratory conditions described earlier. Both survival curves show a rectangular character typical of animal populations manifesting senescence, namely, a very low mortality rate during the early days of the cohort's existence, and a middle period of rapid dying off. However, during the final five to ten per cent of the

population's existence the survival curves for both sexes show a logarithmic-like character (in the extremely retarded rate of dying off of this small proportion of long-lived members of the population). In actual fact, for the males about 90 per cent die off during the period of ten to thirty days after

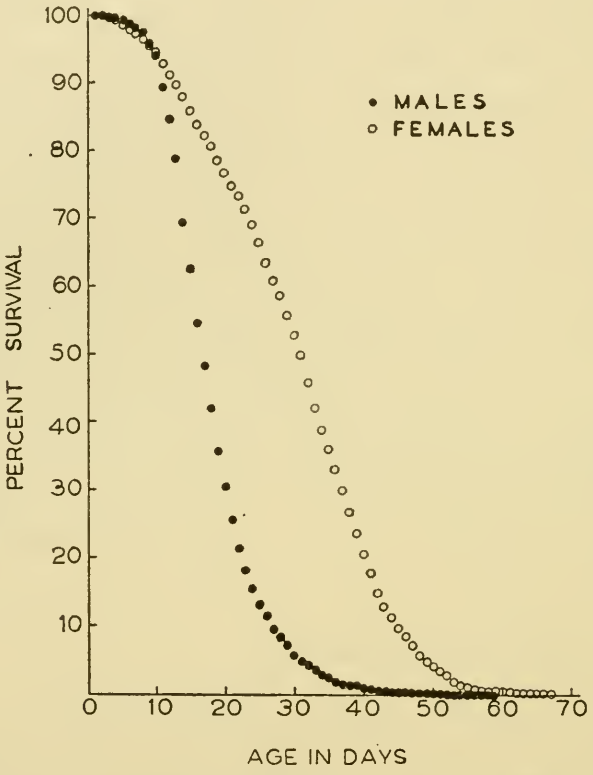


FIG. 2. Survival curves of male and female houseflies.

Reprinted from Rockstein and Lieberman (1958), by courtesy of the Editor, *Nature*.

emergence as adults; for females this period of "senescence" occurs during the longer period of ten to fifty days of adult life.

One striking feature of the particular colony studied is the remarkable homogeneity of the population, as regards longevity at least. Thus, both for the total 600 flies per sex,

from the earlier study on diet (Rockstein, 1957), and the more recent total of over 4,000 flies per sex, fifty per cent mortality occurred at 16 days for the males and at 30 days for the females, respectively. The *mean* longevity values for males of about 17 days and for females of about 29 days, for this large

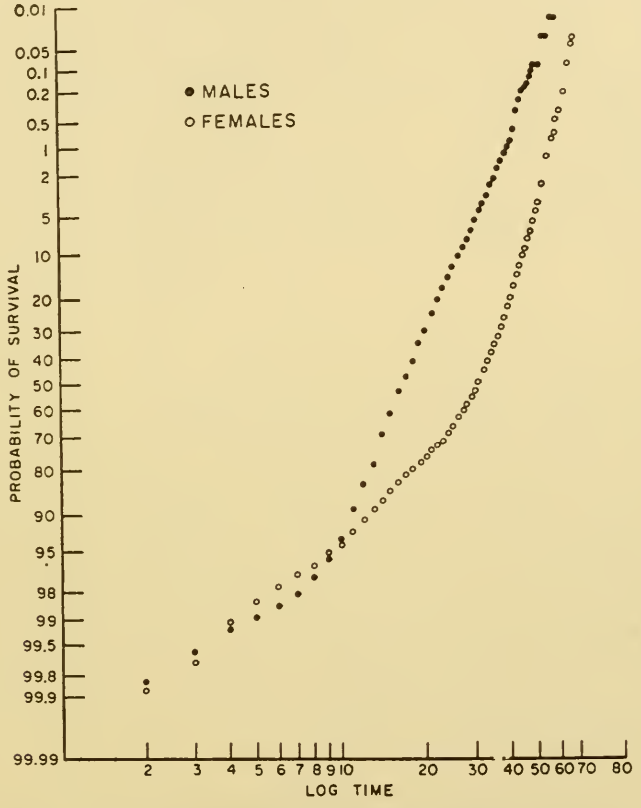


FIG. 3. Log-probit plot for male and female housefly survival.

Reprinted from Rockstein and Lieberman (1959), by courtesy of the Editor, *Nature*.

number of flies, also compare favourably with those reported in 1957. The close approximation of mean and medium longevity values is also a strong indication of a good natural distribution in so far as the populations of the two sexes in this strain are concerned.

A log-probit plot of these data (probability of survival

plotted against time), shown in Fig. 3 (Rockstein and Lieberman, 1959), portrays in more dramatic fashion the actual course of the survival (or, conversely, the mortality) trends of Fig. 2, above. From the similar flat slopes of the log-probit curves of both males and females during the first ten days, a similar low mortality rate is apparent. After the tenth day, however, a marked shift upward of the male curve, which continues as a straight line through the fortieth day, represents a high and uniform mortality rate during 93 per cent of the male population's existence. Thus a single (or at least relatively simple) mortality factor appears to be operating in the great majority of the male houseflies of this strain. In the females, however, one sees that the same log-probit curve follows a more irregular course, with a slight upward trend at the tenth to 21st days, a steep shift upward at the 21st day, another more gentle upward rise in slope at the 30th, and a final shift upward at the 40th day, which persists unchanged as a steep, straight line from the fortieth to final day of the female population's existence. One might infer from this kind of plot that, for the female, mortality (and therefore survival) is a much more complex phenomenon, with more factors for mortality becoming effective with increasing age. These inferences have been further substantiated in the life-tables which have been recently completed by Rockstein and Lieberman (1959) from mortality data for this population of male and female flies. Despite the wide distribution of the ubiquitous housefly, only a few other studies have been made on its longevity. The study of Wilkes and co-workers (1948) employed the Peet-Grady method (in which some of the dietary components are not standard) and obtained average longevities of 12 days for males and 20 days for females of a laboratory strain and about 12 days and 24 days, respectively, for male and female flies of a wild strain, kept at 80° F and 50 per cent relative humidity. Aside from dietary variation, the authors also describe major difficulties of overcrowding, especially in the larval stage and also for adults. In a recent letter, Rollins (1959) has supplied

some interesting data on differences in longevity between the sexes for over 2,000 males and females of a 15-year inbred strain of normal houseflies, originating from a wild strain collected in the Sacramento, California, area, and reared and maintained on a Peet-Grady medium at 80° F. For male houseflies, he obtained a 50 per cent mortality at 11 days (as opposed to our values of 16 days) and for females at 29·5 days (very much like our own data for females). Thirty-day mortalities of 98 per cent for males and 52 per cent for females corresponded very closely to those obtained for our own NAIDM strain. For the Levant house-fly, *Musca vicina* Macq., however, Feldman-Muhsam (1944) and Ascher and Levinson (1956) found no significant difference in longevity between the two sexes.

Parental age

In an attempt to establish the possible effect of parental age of houseflies at oviposition upon the longevity of the offspring, a preliminary investigation was made according to the procedure of Lansing (1947, 1948, 1954). For standard breeding and in all previous studies, eggs were collected from parents at the youngest possible age (at the fourth to fifth day after emergence). In this series of experiments, however, 225 eggs each were collected at the fourth, sixth, ninth, 15th, 23rd and 27th days and the offspring otherwise reared and maintained as before on complete diets. Table III shows that the female offspring longevity is progressively diminished with advancing age of the parents at the time of oviposition; e.g. survival, as expressed as 30-day mortality for female offspring, falls from 50 per cent mortality for eggs from young parents, to 92 per cent mortality for eggs laid at 27 days of parental life. The 30-day mortality data for male offspring, on the contrary, were interpreted as meaning that male offspring longevity was unaffected by increasing parental age. Values also included in Table III show corresponding declines in average longevities for females from about 32 days for

young parents to 22 days for females from very old parent flies. In the case of Lansing's parthenogenetically reproducing rotifers, his "cumulative reversible aging factor" could be directly attributable to cessation of growth in the old female parent. In the present study, however, several interpretations were possible for the sexually reproducing housefly;

Table III

EFFECT OF PARENTAL AGE OF HOUSEFLIES ON LONGEVITY OF OFFSPRING

Parental age (days)	*Males*	*Females*	
	% Mortality	*% Mortality*	*Average longevity*
4	95	50	32 days
6	93	52	29 days
9	97	70	28 days
15	92	82	25 days
23	97	80	24 days
27	90	92	22 days

either or both of the old parents might be contributing to the reduced female offspring longevity which is associated with the advancing age of the parents at oviposition. A second possibility is that the observed data represent the adverse effect of long-term storage of spermatozoa in the female spermatheca. With Dr. Lieberman, an expanded study of the possible rôle of parental age in the longevity of the housefly

was undertaken last year, with four types of matings as follows: young males by old (about 29 days) virgin females, old (about 23 days) males by young virgin females, old males by old virgin females, and "modified old-old crosses" (in which, as in the original study of parental age, males and females were allowed to mate freely from emergence, but where eggs were collected only from parents at an advanced age). A fifth set of cages involved the usual young-by-young matings employed in routine stock breeding and in other studies in which parental age was not a variable; this was the control series. Offspring longevity data were obtained for over 1,000 flies of each sex for each type of cross, for three to four generations in each case, in order to test the possible presence of a Lansing-like, cumulative ageing factor related to parental age, in the housefly. The results obtained indicate that the slightly lowered 30-day mortality for males from oldest parents, seen in our earlier study (Table III), might indeed have been significant. Statistical analysis of data from our current study indicates that, for two generations, the average *male longevity* (20·6 days) for offspring from "modified old-old parents" is higher, by three days, than the mean longevity for young-by-young crosses (P is less than 0·01). That this result may be due to the effect of the female parent upon male offspring is supported by the observation that a similar increase in male offspring longevity was obtained for crosses between young males and *old virgin females* and for two cases of crosses between old males and *old virgin females*. Thus, the mechanism involved may be one of selection of a long-lived strain of male offspring from the longer-lived female parents surviving to almost 30 days of age and still sexually functional at that advanced age. As for the effects of parental age on *female offspring longevity*, data obtained in this more recent and extensive study suggest that the parental ageing effect on this sex is more complex: it is considered essential at this point to continue these studies with single-pair crosses in order to follow the longevity of the adults as

well as of their offspring on an individual, rather than on the group population basis employed in all studies to date.

In *Drosophila subobscura* Comfort (1953) found no appreciable change in longevity of the population resulting from selection of eggs from old parents, over eight generations of breeding. Tracey (1958), on the other hand, found that larvae of eggs from week-old adult beetles of the mealworm, *Tenebrio molitor*, had longer developmental periods than those from eggs laid by five-week-old (middle-aged) beetles and considerably longer than those from eggs laid by very old (nine weeks) parents. The adult lifespan was likewise shortened for beetles reared from eggs laid by oldest parents. Thus, as the parental age lengthened, the entire lifespan of offspring was shortened in this species. Although the above held true for animals reared and maintained at 25°c, at 30° c some larvae from oldest parents had much longer larval development periods than those from younger parents (!). However, increasing the temperature to 30° c did not alter the shorter adult lifespan observed for offspring from oldest parents.

What rôle the age of parents plays in the lifespan of children in humans is not statistically clear, although Murphy (1954) reported that known abnormalities like congenital cardiac impairment, Mongolian idiocy, spina bifida and stillbirth, and possibly hairlip and cleft palate, increase in frequency as the age of the mother at the time of birth increases, after 30 years of age. However, Sonneborn (1957) has pointed out that the age of the mother is frequently positively correlated with the *paternal age*, for foetal deaths. Indeed, for data covering foetal deaths and a 10 per cent randomized sample of 330,000 live births from 1954–55 New York City Department of Statistics, he found there was a consistently higher foetal death rate for older fathers, when single rather than five-year age classes were employed for females over 30 years of age.

Summary

Queenless, Italian golden worker honey-bees, *Apis mellifera*, maintained indoors on an excess of honey, pollen and water, lived to a maximum of about 9·5 weeks; in a second study of over 4,000 bees a similar maximum value of ten weeks was obtained. A maximum longevity of 7·5 weeks was found for over 2,700 bees, properly marked and returned to the hive to perform normal hive activities. As a criterion of old age, the number of brain cells at two distinct levels of the adult honey-bee brain was found to be virtually identical for both indoor and outdoor (hive) senescent bees.

In a study of over 8,500 houseflies, *Musca domestica*, of the NAIDM strain, females were found to have a mean longevity of 29 days and males a mean longevity of 17 days. Curves for probit-log time plots indicated a relatively simple mortality factor for the male population but a complex of several mortality factors for the female cohort. Female longevity was enhanced by the inclusion of powdered whole milk in the adult diet of sugar and water. No such beneficial effect was obtained for male houseflies. A study of the rôle of parental age at the time of oviposition indicated a possible adverse effect on the longevity of female offspring from oldest parents; *for males* reared from eggs from oldest parents there appears to be an *enhancement* of the mean longevity, probably by a selection of long-livedness through the old surviving female parents.

Acknowledgements

Figs. 1*a* and 1*b* were drawn by Miss Mary Lorenc.

Fig. 3 was drawn by Mr. Rudolph Cavalcante.

The author is deeply appreciative of the assistance of Dr. Albert S. Perry of the USPHS Technical Development Laboratories, Savannah, Georgia, for generously supplying the pupae of the NAIDM strain from which this colony has been developed.

The kind assistance of Miss Gertrude Uhr, Secretary of the Department of Physiology, and Mrs. Elaine S. Rockstein, in the preparation of the manuscript, is acknowledged.

The research described in this report was supported in part by the United States Army Surgeon General's Office and the United States Public Health Service Division of Research Grants.

REFERENCES

ANDREW, W. (1938). *Z. Zellforsch.*, **28**, 294.
ASCHER, K. R. S., and LEVINSON, Z. H. (1956). *Riv. Parassit.*, **17**, 217.
COMFORT, A. (1953). *Nature* (*Lond.*), **172**, 83.
ELLIS, R. S. (1919). *J. comp. Neurol.*, **30**, 329.
ELLIS, R. S. (1920). *J. comp. Neurol.*, **32**, 1.
FELDMAN-MUHSAM, B. (1944). *Bull. ent. Res.*, **35**, 53.
GARDNER, E. (1940). *Anat. Rec.*, **77**, 529.
GROSCH, D. S. (1950). *Biol. Bull., Wood's Hole*, **99**, 65.
HATAI, S. (1902). *J. comp. Neurol.*, **12**, 107.
HAYDAK, M. H. (1953). *Ann. ent. Soc. Amer.*, **46**, 547.
HODGE, C. F. (1894). *J. Physiol.*, **17**, 129.
INUKAI, T. (1928). *J. comp. Neurol.*, **45**, 1.
LANSING, A. I. (1947). *J. Geront.*, **2**, 228.
LANSING, A. I. (1948). *Proc. nat. Acad. Sci.* (*Wash.*), **34**, 304.
LANSING, A. I. (1954). *Ann. N.Y. Acad. Sci.*, **57**, 455.
MAURIZIO, A. (1954). *Landw. Jb. Schweiz.*, **68**, 115.
MCCAY, C. M., and CROWELL, M. F. (1934). *Sci. Mon., N.Y.*, **39**, 405.
MCCAY, C. M., CROWELL, M. F., and MAYNARD, L. A. (1935). *J. Nutr.*, **10**, 63.
MCCAY, C. M., MAYNARD, L. A., SPERLING, G., and ASGOOD, H. S. (1941). *J. Nutr.*, **21**, 45.
MCCAY, C. M., MAYNARD, L. A., SPERLING, G., and BARNES, L. L. (1939). *J. Nutr.*, **18**, 1.
MURPHY, D. P. (1954). *Ann. N.Y. Acad. Sci.*, **57**, 451.
ROCKSTEIN, M. (1950*a*). *J. cell. comp. Physiol.*, **35**, 11.
ROCKSTEIN, M. (1950*b*). *Ann. ent. Soc. Amer.*, **43**, 152.
ROCKSTEIN, M. (1953). *Biol. Bull., Wood's Hole*, **105**, 154.
ROCKSTEIN, M. (1956). *J. Geront.*, **11**, 282.
ROCKSTEIN, M. (1957). *J. Geront.*, **12**, 253.
ROCKSTEIN, M. (1958). *J. Geront.*, **13**, 7.
ROCKSTEIN, M., and LIEBERMAN, H. M. (1958). *Nature* (*Lond.*), **181**, 787.
ROCKSTEIN, M., and LIEBERMAN, H. M. (1959). *Gerontologia* (*Basel*), **3**, 23.
ROLLINS, R. Z. (1959). Personal Communication.
SONNEBORN, T. M. (1957). Proc. Ageing Conference, Gatlinburg. Washington, D.C.: A.I.B.S., in press.
TRACEY, K. M. (1958). *Ann. ent. Soc. Amer.*, **51**, 429.
WILKES, A., BUCHER, G. E., CAMERON, J. W. McB., and West, A. S., Jr. (1948). *Canad. J. Res., D.*, **26**, 8.
WOKE, P. A., ALLY, M. S., and ROSENBERGER, C. R., Jr. (1956). *Ann. ent. Soc. Amer.*, **49**, 435.

DISCUSSION

Gerking: Did McCay keep these trout you mentioned until they died? You referred to an increased lifespan for these fish.

Rockstein: My recollection is that he was able to double the lifespan of the trout.

Comfort: The total duration of the experiment was only a matter of months, while they were in the hatchery. The lifespan of trout is at least 10 years.

Berg: The advantage of using rats for lifespan studies is that we can determine causes of death in this species, whereas the pathology of other species has not been studied as thoroughly.

Rockstein: We are not as fortunate as you in having a pathologist. There are insect pathologists, but they are very rare and very costly.

Berg: McCay employed drastic underfeeding so that his animals were severely retarded in growth and did not attain sexual maturity. The greater longevity of McCay's rats has been attributed in part to the retardation of sexual development. In our experiments, sexual maturity of the females was delayed only three to four weeks, and skeletal measurements were only 5 to 7 per cent less than in *ad libitum*-fed rats. These findings indicate that longevity of the rat can be increased by dietary restriction without seriously affecting skeletal growth or sexual maturity.

Rockstein: We are all eagerly awaiting the results of your experiments on longevity.

Comfort: I am a little disturbed, Prof. Rockstein, about drawing analogies between the nutritional requirements of rats and those of insect imagos. For example, I take it there is very little extragonadal mitosis in your flies. Any change you get is not due to altering the number of cell generations or the stage of development.

Rockstein: No, I did not mean to draw that analogy. I should have mentioned that adult flies are essentially fully-grown animals, much like the honey-bee, but even more so because the honey-bee takes about ten days to attain full maturity. The housefly on the other hand is completely mature within a few hours except for the ability to lay fertile eggs, under standard laboratory conditions. But I did mean very definitely to compare the human with the rat, and to emphasize that starvation would hardly be of any use in the human if one wanted to prolong life. I do not know that it has ever been shown to do so; if anything, it would shorten the lifespan in man. When McCay and his workers came out with the pronouncement that a low protein, low calorie diet was what we needed for a

long life, I thought that was rather a broad inference from their particular study on white rats.

Comfort: I do not think any human population has ever been subjected to the sort of controlled and selective restriction of diet which Dr. Berg and Prof. Simms have been using. Starved populations are deficient in all foods, and do not receive adequate vitamin supplements, as McCay's rats did. There is a difference there. I agree with you entirely about the general principle.

Sacher: Restrictions in diet during and after the past war in several countries may have had a relation to the observed decrease in mortality from heart disease.

Tanner: In some of the degenerative diseases, for example diabetes, the incidence and the death rates went down, But this is different from the notion that at the same time children are being starved and therefore they might live longer later on. The starvation during the war lasted a sufficiently short time, so that those children who were starved probably picked up on to their natural growth curves a little later on. It was acute or sub-acute starvation, which is probably compensated for pretty rapidly. We know that the human, like the rat, gets back to the normal growth curve fairly rapidly, even after severe disease or severe starvation. It is for this reason that I do not think this data is particularly relevant.

Sacher: Nevertheless, such children constitute a cohort which can be followed in successive decades. Even though normal growth is resumed, there may still be permanent after-effects detectable in later susceptibility to disease.

Jalavisto: Did you measure the death rate at earlier dates in this parental age series, Prof. Rockstein?

Rockstein: Yes, I have curves, but this was a very limited study, involving about 150 flies in each case, and so the data are not really adequate for preparing such curves.

Maynard Smith: My colleague Miss Clarke has been doing experiments on the effect of larval nutrition on the longevity of *Drosophila*. The animals are kept as adults in the same environment on the same food, but are fed as larvae on diets varying from 0·03 per cent up to about 16 per cent of dead yeast. I do not think she would want to commit herself very much on the results, because she has not finished doing the sums. However, it is quite clear that the effect, if any, of larval nutrition on adult longevity is very small. It has an effect on the time it takes the animals to develop, and on how big they are when they emerge from the pupae, but it has only a very tiny effect on their adult survival in either sex. I confess I find that surprising.

Rockstein: Do they lay eggs?

Maynard Smith: Yes. The more protein you give them as larvae, the higher the rate of egg-laying when they are adults. We therefore suspected that the ones which had a lot of protein might not live as long as the others, but there is no overall effect of any great magnitude. If there is an effect it is of the order of 10 or 20 per cent—not more than that.

Kershaw: There is an analogous situation in parasitism. The ability of the tsetses to act as vectors of sleeping sickness is largely determined by the temperatures at which the pupae are maintained before the adults come out. What effect that has on the longevity of the adult is not known, but it will be a sort of parallel viability, or parallel parameter that we put against longevity.

It is the middle-aged insect which is the important survivor for parasites, because the ones which die young do not live long enough to transfer the parasite. Secondly, a very complex pattern of mortality is evident in the development of a parasite in different selected organs of an insect. A third point is the ability of the insect to support the parasite, so that those at the tag end of their life cannot act as vectors. That has an obvious application in the field but what this means biologically one does not know. Unfortunately there are no means at the moment of quantitatively assessing the capacity of insects to support some parasites.

Wigglesworth: Could you describe the sexual difference in the effect of protein feeding by saying, rather as Prof. Kershaw is implying, that the adult male is not protein-starved, but that the adult female is starved of protein by its reproductive activities—therefore in the absence of the extra protein feeding it succumbs early?

Rockstein: Yes, that inference would be very appropriate.

Sacher: I found a survivorship curve for male *Drosophila* almost identical with what you found for the male housefly, Prof. Rockstein. Unfortunately I did not get data for female *Drosophila.* In regard to your remarks about the complexity of the survivorship curve for the female (and I think we should say for the male too), perhaps we should recall the controversy between Crozier and Pearl (Pearl, R., White, P., and Miner, J. R. (1929). *Proc. nat. Acad. Sci.* (*Wash.*) **15,** 425). Pearl had studied the resistance of *Drosophila* to alcohol as a function of age and he got a curve which he graduated smoothly. Crozier (Crozier, W. J., Pincus, G., and Zahl, P. A. (1936). *J. gen. Physiol.*, **19,** 523) objected that such smoothing was not proper and he did a far more extensive experiment. He established that the resistance of *Drosophila* to alcohol as a function of age went through many stages and was an exceedingly complex curve. This comes

back to the fact that we must eventually dissect the life-table into several components, as Dr. Benjamin has pointed out, and as H. S. Simms (1940. *Science*, **91**, 7) has shown previously.

Brauer (personal communication) at the Naval Radiological Defence Laboratory in San Francisco is using McCay's technique now. He re-feeds rats at various ages and finds that the rate of growth when full feeding is re-established carefully is preserved up to quite late ages, and then diminishes. This is somewhat like Comfort's regeneration and re-feeding experiments. Brauer is also examining the effect of previous X-irradiation on the ability to resume growth.

Rockstein: McCay could accelerate senescence in an old animal which appeared to be young because of starvation. By re-establishing the full diet, the animal's appearance rapidly shifted to that of an old animal and mortality was accelerated.

THE RATE OF AGEING IN *DROSOPHILA SUBOBSCURA*

J. Maynard Smith
Department of Zoology, University College London

To a geneticist, the oddest feature of gerontology is the absence of a coherent and generally accepted theory of ageing, comparable to the chromosome theory of heredity. In case this remark should cause any misgivings, it should be said that no attempt will be made to remedy this defect. Instead, two kinds of theory which seem to be possible will be indicated, since this will help to interpret some experiments to be described later.

We have to accept that a theory of ageing may be valid only for a single species or group of related species. It may be that we shall find a theory which proves to have the same universality in the study of ageing as does the chromosome theory in genetics, but this does not at present seem very likely. What kinds of theory, then, can be put forward to explain ageing in a single species, say in men or in mice or in fruitflies? A distinction should be made between two types of theory, which may be called "single" and "multiple" theories of ageing.

A multiple theory would postulate that there are a number of partially independent processes occurring in every individual, any one of which may ultimately cause death. It is not intended to imply that two processes in a single individual can ever be wholly independent; by "partially independent" is meant only that each process would continue, perhaps at an altered rate, in the absence of the others. Now some ageing processes are fairly certainly independent in this sense. For example, the mechanical wearing away of the teeth of herbivorous mammals would occur even if other

ageing processes were arrested, and, unless there is continuous tooth growth, would ultimately lead to death. Similarly, in so far as cancer is the result of cumulative environmental insult, it is partially independent of other ageing processes, though it would be rash to assume that it is wholly so. But it is always possible that apparently unrelated symptoms of ageing may be due to a single cause, just as apparently unrelated abnormalities of development may be the pleiotropic effects of a single gene. A "single" theory would postulate that all or most of the symptoms of ageing are the consequence of a single process (or of a single series of processes), either at a cellular or organism level.

There is one observation which at first sight appears to support such a single theory. In a given species, the deterioration of different organ systems proceeds at roughly the same rate; if this were not so, individuals dying of "old age" would always die of the same immediate cause. This synchrony might suggest a high degree of physiological interdependence, with some one particular process acting as a timekeeper. But the synchrony can be explained in another way. Suppose that ageing in mammals is in fact multiple in character. Then if in any species one ageing process, say the deterioration of the central nervous system, proceeded at a much higher rate than did other ageing processes, there would be strong natural selection tending to slow down the rate of ageing in this system, if necessary at the expense of accelerating other ageing processes. In other words, natural selection will tend to synchronize different ageing processes, even if these are physiologically independent of one another. The example of tooth wear already mentioned demonstrates that selection can in fact act in this way. The volume of tooth worn away in unit time is proportional to the volume of food eaten, which in turn is roughly proportional to the surface area of the animal. Consequently, the expectation of life of the teeth of small mammals is less than that of large mammals. However, many small herbivores (rodents) have

evolved molar teeth which grow throughout life, whereas large herbivores have not. Similarly, the age of onset of cancers in species with different life expectancies (say in mice and men) is roughly proportional to those expectancies, and this proportionality seems more likely to be a consequence of synchronizing selection than of a direct physiological connexion between ageing generally and cancer.

It follows that a decision between a single and a multiple theory in any species is impossible without experimental

Table I

MEAN SURVIVAL TIMES IN DAYS OF ADULT FLIES AT VARIOUS TEMPERATURES

Temperature °C.	*Males*			*Females*		
	No. of flies	*Survival time in days*		*No. of flies*	*Survival time in days*	
20	50	67·4 ± 2·46		50	55·9 ± 2·58	
25 raised at 15°	25	29·5 ± 1·07	27·05	25	40·5 ± 1·68	35·55
25 raised at 25°	25	24·6 ± 1·10		25	30·6 ± 1·65	
30·5	50	7·58 ± 0·28		50	17·60 ± 0·65	
33	10	0·79 ± 0·08		10	0·82 ± 0·05	

interference with the process. The grafting of organs from young individuals into old and *vice versa*, or between individuals with different genetically determined rates of ageing, is perhaps the most promising experimental approach (Jones and Krohn, 1959; Medawar, 1957). Some experiments will now be described on ageing in *Drosophila subobscura*, using a different approach, but leading to the conclusion that the ageing process is a multiple one (Maynard Smith, 1957, 1958).

It has been known for a long time that in poikilothermous animals the expectation of life decreases with increasing temperature. It was the purpose of the investigation now to

be described to discover how far the processes responsible for death in *D. subobscura* are the same at different temperatures, differing only in the rate at which they proceed, and how far different processes are concerned at different temperatures.

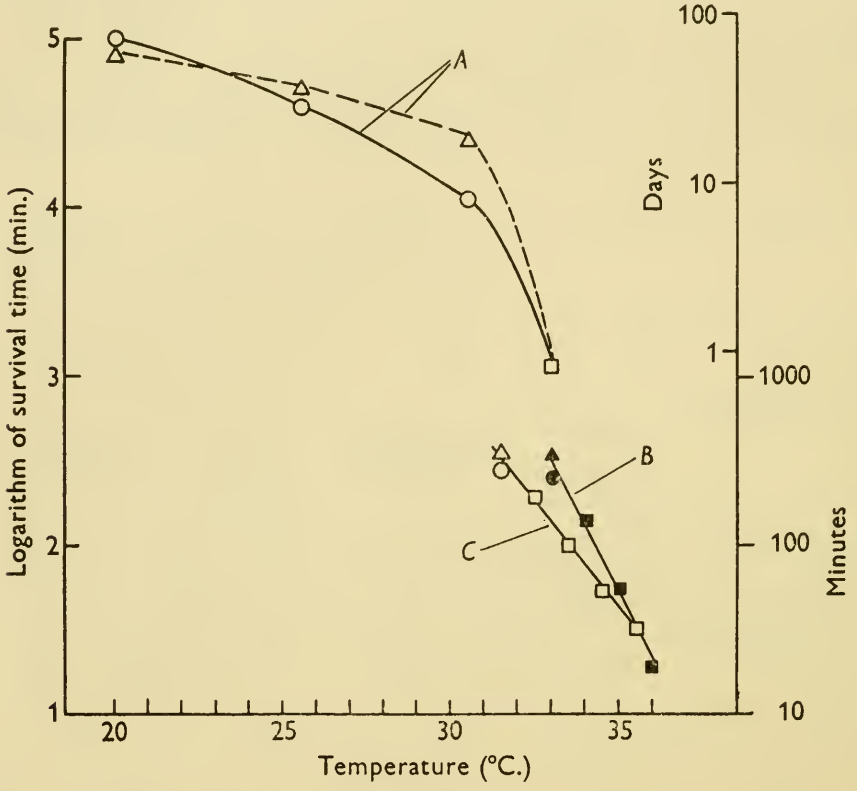


FIG. 1. Survival time of flies at different temperatures. A, in food vials; B, in saturated air; C, in dry air; △, ▲, females; ○, ●, males; □, ■, sexes combined.

Figs. 1–3 and Table II reproduced by courtesy of the Editor, *Journal of Experimental Biology*.

The mean ages at death (measured from adult emergence) of adults kept continuously at various temperatures are shown in Table I. In Fig. 1 these values are plotted on a logarithmic scale, together with the survival times of flies exposed to higher temperatures without food or water in dry and in saturated air. The rather sudden change in the slope of the curve in Fig. 1 suggests that the causes of death at high

temperatures may be different from those acting below about 31°. This suggestion is confirmed by the finding that the changes which occur at high temperatures are, wholly or in part, reversible, whereas the changes which occur at 30·5° are irreversible.

The reversibility of a change is judged by exposing individuals to high temperatures intermittently, with intervening periods at a lower temperature. Thus if flies are exposed to a high temperature (33·5° in dry air or 34·3° in saturated air) for 50 minutes (i.e. for about half their expectation of life at that temperature) and are then kept for three hours at 20°, their survival times when they are again exposed to the high temperature are as great or greater than the survival times of flies not previously exposed. Thus death in these conditions is due to changes which can be reversed at a lower temperature; therefore the changes responsible for death at high temperatures are not regarded as processes of senescence. Experiments in which flies were kept in food vials alternately for eight hours at 33° and for 16 hours at 20° showed that the changes responsible for death at 33° in food vials are also in part reversible.

In contrast, as is shown in Table II, the changes responsible for death at 30·5° are not to any appreciable extent reversed at lower temperatures. There is evidence for a small degree of recovery in males, since the first eight-day interruption at 20° did slightly increase the further expectation of life at 30·5°, although the second interruption did not. Females which were exposed intermittently had total survival times which were if anything slightly shorter than those of flies exposed continuously.

Since the changes responsible for death at 30·5° are, at least in the females, irreversible, and since they take an appreciable time to reach completion (mean of 17·6 days for females), it seems reasonable to regard them as processes of ageing. The question then arises, are they the same processes as are responsible for ageing at 20°? If the processes of ageing

at the two temperatures were in fact identical, it would be possible to predict the total lifespan of flies kept for varying periods at the two temperatures. For example, a female exposed for eight days to 30·5° soon after emergence would

Table II

EXPECTATION OF LIFE AT 30·5° C.

	No. of flies	*Further expectation of life at 30·5° (days)*
Females		
(1) Exposed continuously to 30·5°	50	17·60 ± 0·65
(2) After 5 days at 30·5°		
(a) Exposed continuously	50	12·60 ± 0·65
(b) 8-day interruption at 20° after 5 days at 30·5°	25	11·02 ± 0·28
(3) After 13 days at 30·5°		
(a) Exposed continuously	44	5·82 ± 0·49
(b) 8-day interruption at 20° after 5 days at 30·5°	25	3·02 ± 0·28
(c) Two 8-day interruptions at 20° after 5 and 13 days at 30·5°	22	5·23 ± 0·32
Males		
(1) Exposed continuously to 30·5°	50	7·58 ± 0·28
(2) After 5 days at 30·5°		
(a) Exposed continuously	49	2·64 ± 0·27
(b) 8-day interruption at 20° after 5 days at 30·5°	44	5·23 ± 0·38
(3) After 8 days at 30·5°		
(a) Exposed continuously	21	1·40 ± 0·35
(b) 8-day interruption at 20° after 5 days at 30·5°	36	2·97 ± 0·36
(c) Two 8-day interruptions at 20° after 4 and 8 days at 30·5°	25	2·42 ± 0·23

be expected to have completed about half its expected lifespan, and therefore to have a further expectation of life at 20° of about 28 days. Experiments do not confirm this simple additive hypothesis.

Fig. 2 and Table III show the results of exposing young adult females to 30·5° for varying periods, and then keeping

them at 20° until they died. The exposure, so far from decreasing their expectation of life, in fact increased it, by as much as 50 per cent in females exposed for eight days. In a similar experiment, a group of males were exposed to 30·5° for five days, or two-thirds of their expectation of life at that temperature. The further expectation of life of these males at 20° did not differ from that of a group of unexposed controls.

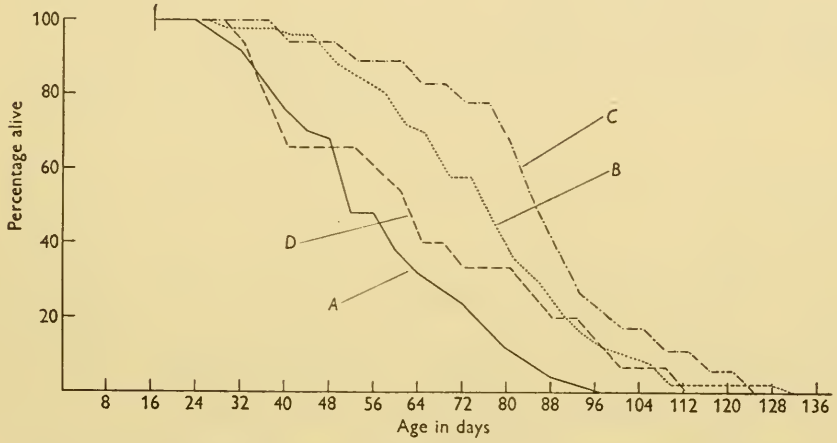


FIG. 2. Survival time at 20° of females previously exposed to 30·5°. A, unexposed; B, exposed for 5 days; C, exposed for 8 days; D, exposed for 12 days.

It follows that, both for males and females, different processes are responsible for death at the two temperatures; we are therefore obliged to accept a multiple theory of ageing for this species. The situation is further complicated by the different response of males and females to exposure to 30·5°, which prolonged the life of females but left that of males unaltered. The clue to this difference was found when it was observed that exposure to a high temperature caused a partial regression of the ovaries of females, which subsequently laid eggs at only about half the rate of unexposed females. This suggested that the process of egg-laying might accelerate ageing in females, and that the exposure to a high

Table III

EXPECTATION OF LIFE IN DAYS OF FEMALES KEPT AT 20° C.

	No. of flies	*Further expectation of life in days at age 17 days*
Kept continuously at 20°	50	38·9 ± 2·6
Exposed to 30·5° for 5 days (6th to 10th day after emergence)	47	57·2 ± 3·0
Exposed to 30·5° for 8 days (6th to 13th day after emergence)	18	67·8 ± 4·9
Exposed to 30·5° for 12 days (6th to 17th day after emergence)	15	50·0 ± 6·6

temperature prolongs life because it slows down the rate of egg-laying.

This suggestion has been confirmed by experiments using virgin females (which lay eggs at a reduced rate), and females lacking ovaries. The latter were obtained by using females homozygous for the mutant "grandchildless" (Spurway, 1948), whose offspring appear to be normal in all respects

Table IV

EXPECTATION OF LIFE OF FEMALES KEPT AT 20° C.

	No. of flies	*Further expectation of life in days at age 10 days*
MATED FEMALES		
kept continuously at 20°	48	33·1 ± 1·6
exposed to 31° for 5 days	23	61·2 ± 5·7
VIRGIN FEMALES		
kept continuously at 20°	89	58·7 ± 2·7
OVARILESS FEMALES		
kept continuously at 20°	28	67·6 ± 4·7
exposed to 31° for 3 days	22	64·2 ± 5·6

except for the absence of gonads. The results of these experiments are shown in Fig. 3 and Table IV. As before, the exposure of normal mated females to a high temperature increased their expectation of life at 20°. As would be expected from the hypothesis being tested, both virgin and ovariless females lived for longer than did the controls, and closely resembled the females exposed to a high temperature. The final confirmation of the hypothesis comes from the fact

FIG. 3. Survival time of females at 20°. A, normal mated females; B, ovariless females; C, normal virgin females; D, normal mated females exposed for 5 or 6 days to 31°.

that the expectation of life of ovariless females, as of males, is not increased by exposure to a high temperature; since such females will not lay eggs in any case, exposure cannot further prolong their life. The greater longevity of virgin as compared to mated females has previously been demonstrated by Bilewicz (1953) in *Drosophila melanogaster*, and by Griffiths and Tauber (1942) in *Periplaneta americana*.

It is natural to suppose that the causes of ageing of ovariless or virgin females at 20° are the same as the causes of ageing of males at the same temperature. But these experiments leave one question unanswered. Does egg-laying shorten the life

of females because it accelerates processes which occur in any case in ovariless females, or is it a process which would by itself ultimately result in death, even if other ageing processes could be arrested? We are again faced by a choice between a single and a multiple theory. As yet we have not been able to find a way of deciding between them, but we hope we may be able to do so by studying ageing in genetically different strains on varying diets, since in this way we have other means of altering both the rate of ageing and of egg-laying.

Table V

The longevities of inbred and of outbred flies in days at 20° c.

		Mean lifespan		*Coefficient of variation*	
		Females	*Males*	*Females*	*Males*
Nine inbred lines	range	17·2–53·8	17·1–69·2	0·35–0·69	0·35–0·66
	mean	36·4	40·0	0·51	0·55
Four outbred populations	range	55·9–64·1	44·7–67·4	0·29–0·35	0·23–0·50
	mean	60·0	56·8	0·32	0·33

We may now turn to the genetics of ageing in *D. subobscura*. Our interest in ageing originated with the discovery (Clarke and Maynard Smith, 1955) that the hybrids between inbred lines live for longer, and are less variable in lifespan, than their inbred parents. These findings have been confirmed by later work (Table V), although we were perhaps fortunate that the particular pair of inbred lines originally available for study showed the effect in a particularly striking manner. But later work has shown that, in addition to genetic variance due to "heterosis" or "overdominance", much of the genetic variance of longevity is due to genes with sex-limited effects, i.e. to genes with different effects on the longevity of males and

of females (Maynard Smith, 1959). This can be shown in two ways. Table VI shows the lifespans of males and of females of nine inbred lines, two kinds of F_1 hybrids between inbred lines, and the offspring of two groups of wild-caught females, one from Kent and one from Galilee. In eight of these 13 populations there was a significant difference between the

Tables VI

RELATIVE LONGEVITIES OF MALES AND FEMALES, IN DAYS, AT 20° C.

	Lifespan			
	Females	*Males*	*Ratio*	*P*
INBRED LINES				
K	17·2	31·2	0·55	++
M	35·3	51·8	0·68	+
F	53·8	69·2	0·77	+
O	48·7	52·5	0·93	
NFS	40·7	42·4	0·98	
D	50·2	47·5	1·06	
B	33·3	25·8	1·29	+
G	30·0	22·6	1·33	+
E	36·2	17·1	2·12	++
F_1 HYBRIDS				
K/NFS	55·9	67·4	0·83	++
B/K	61·5	61·6	1·00	
OFFSPRING OF WILD FLIES				
Kent	58·6	53·4	1·10	
Galilee	64·1	44·7	1·43	++

++, significant at 0·001 level; +, significant at 0·10 level.

longevities of the two sexes, but in four cases it was the males and in four cases the females which lived for longer. This can only be explained by the presence of genes which affect the longevity of the two sexes differently. The same conclusion emerges from a study of the correlations between the longevities of relatives in a population derived from females caught in Galilee (Table VII). All the correlations are rather low; this means only that many differences between members of the

population were due to uncontrolled variations in environmental conditions. But all the correlations between relatives of like sex were significant and positive, whereas only one of the four correlations between relatives of unlike sex was significantly different from zero.

The presence of sex-limited genetic variance of longevity is understandable in view of the physiological findings described earlier. Since the causes of ageing in males and in females are

Table VII

CORRELATIONS BETWEEN RELATIVES AMONG THE DESCENDANTS OF FEMALES CAUGHT IN GALILEE

	Like sex		*Unlike sex*
Brother-brother F_1	0·13		
Brother-brother F_2	0·19		
		Brother-sister F_1	0·04
		Brother-sister F_2	0·04
Sister-sister F_1	0·12		
Sister-sister F_2	0·20		
Father-son	0·29	Father-daughter	0·19
Mother-daughter	0·15	Mother-son	−0·04

at least in part different, it is to be expected that gene differences should exist with different effects on the longevity of the two sexes. The moral seems to be that the genetics of a character can often be better understood if something is known of its physiology.

To sum up, the most important conclusion which has emerged from this work seems to be that ageing in *Drosophila subobscura* is "multiple" in character. The processes responsible for death at 30·5° are reasonably regarded as processes of "ageing" or "senescence", since they are not reversed or repaired at 20°, and since they take an appreciable time to reach completion. Yet they are not the same as the processes responsible for ageing and death at 20°. Further, the process of egg-laying either accelerates the normal

ageing processes of females at 20°, or is itself an age processing capable independently of causing the death of females.

REFERENCES

Bilewicz, S. (1953). *Folia biol. (Kraków)*, **1**, 177.
Clarke, J. M., and Maynard Smith, J. (1955). *J. Genet.*, **53**, 172.
Griffiths, J. T., and Tauber, O. E. (1942). *Physiol. Zoöl.*, **15**, 196.
Jones, E. C., and Krohn, P. L. (1959). *Nature (Lond.)*, **183**, 1155.
Maynard Smith, J. (1957). *J. exp. Biol.*, **34**, 85.
Maynard Smith, J. (1958). *J. exp. Biol.*, **35**, 832.
Maynard Smith, J. (1959). *J. Genet.*, in press.
Medawar, P. B. (1957). The Uniqueness of the Individual. London: Methuen.
Spurway, H. (1948). *J. Genet.*, **49**, 126.

DISCUSSION

Danielli: There may be an alternative explanation for your experiments to the one you suggest, namely that the causes of ageing are multiple. In the study of cell division it is now common practice to synchronize cells by giving them a cycle of temperature changes. The logic behind this is that the synchronization is due to the breaking of a cycle or to interference with some phase of the cycle of metabolic activity, so that when the constraint due to temperature change is removed, all the cells take up a new cycle at the same point. In your animals the variance decreased in some of the experiments, which would suggest that some measure of synchronization was occurring. You may fail to get the additive effect one expects in ageing, not because the cause of death is different at different temperatures, but because you break the initial ageing cycle by moving from one temperature to another and then later the animals begin somewhat closer to the origin of a cycle than they would have done had you kept them constantly at one temperature. This would mean that there is possibly only one cause of death, although they are behaving as if there were two causes.

Maynard Smith: I would accept that as a very possible explanation of the reduction in variance of the population exposed to 30·5° intermittently, compared to that exposed continuously. We shall have to repeat the experiment which showed this striking reduction in variance to see whether it was just one of those things that happen once, or whether it will happen every time. But I would not accept your suggestion as an alternative to the existence of the two processes of ageing. After eight days at 30·5° one knows that, although all the animals are alive, they are all actually "half dead". They are all

halfway through a programme towards death, and if left at that high temperature most of them would be dead in another eight days. If it was the same programme which is responsible for death at 20°, then one would expect that flies exposed for eight days to 30·5° and then kept at 20° until they died would behave as if they were halfway through the programme, and not, as actually happens, back at the beginning.

Danielli: I was actually suggesting that the abrupt change of temperature swung the animals back to the beginning of the cycle in each instance. This would mean that you could take the animals halfway through their expectation of life at 30·5° and then the actual change in temperature swings them back to the beginning of their cycle again, or somewhere closer to it.

Maynard Smith: If that were true, one could presumably make them almost immortal. You are suggesting that flies kept at a constant temperature die of physiological boredom.

Sacher: I do not know whether your evidence clearly establishes the hypothesis of multiple as against a single cause of ageing. We had a different experimental situation which leads to results similar to yours. Fruit-flies were given daily doses of X-rays throughout their lives from emergence onwards. Under these circumstances flies that received about 1·5 to 3 kiloröntgens per day throughout life lived more than 30 per cent longer than their controls and at the same time manifested a markedly decreased variance. Subsequently I discovered that W. P. Davey (1917, 1919. *J. exp. Zool.*, **22**, 573; **28**, 447) had also done this with flour-beetles. My interpretation is that X-irradiation is a stress, and that a moderate degree of stress invokes adaptive responses that are not invoked in the animal's natural environment. This leads me to ask whether you could do an experiment in which temperature shocks are given daily or at frequent intervals?

Maynard Smith: I shall have to do such an experiment. Whether you do or do not accept my conclusion that we have a multiple process here hinges largely on whether you accept my argument that what ultimately kills them at the high temperature is properly regarded as a process of ageing. If you just starve a population of *Drosophila* they will all die in about three days, and you will get a survival curve with an increasing force of mortality, looking just like a life-table. But I do not think any of us regard this as a proper process of senescence because it is fully reversible; if you give the flies food after two days' starvation they recover completely. I am arguing that the process at 30·5°, which takes as long as 18 days to reach completion in a fly whose normal life-expectation is only

about 50 days, and which does not seem to be reversible, can properly be regarded as a process of ageing in its own right. Therefore I am rather unhappy about thinking of exposure to 30·5° simply as the application of a stress.

Rotblat: Our own results could be explained by either single or multiple processes, but like Sacher I think your results do not necessarily contradict the single theory. You assume that high temperature produces only ageing processes. But it may cause something else; it may cause trauma or some other process which is not normally present, and consequently it may not be just an ageing process.

Grüneberg: The question of whether we are dealing with single or multiple processes of ageing could probably be tackled by investigating the effects of individual genes on the ageing process. In the experiments you described, considerable differences were found between different inbred strains. These, of course, differ in a multitude of genes and in practice it is impossible to sort out the effects of individual genes following a cross between two inbred strains, as I have repeatedly found in my mouse crosses. It would probably be a better plan to start with single-gene differences. We are about to do that in mice, to see whether genes without obvious pathological effects in some way affect the longevity of the animal. In the mouse this will take about three years, whereas if you are so inclined, you could probably produce significant results in *Drosophila* by Christmas.

Maynard Smith: I certainly could produce results by Christmas. R. Pearl (1928. The Rate of Living. University of London Press) found a long time ago that the gene vestigial in *Drosophila melanogaster* halves the expectation of life. I have no doubt that a number of other genes would alter the lifespan. But I am not a good enough insect pathologist, and to learn anything from such an experiment one should analyse the causes of death.

Grüneberg: The gene vestigial is not a good gene to use because it is itself obviously pathological: because of their reduced wings the vestigial flies tend to get stuck in the food. One should use genes that have no obvious pathological effect.

Maynard Smith: Suppose that you find a particular gene, which is not obviously pathological, but which reduces or extends the life. It would not tell you much unless you could then show that animals with the gene did not die of a specific cause that the others are dying of, or *vice versa*.

Grüneberg: That is exactly what I mean. Once you have shown that a gene affects the lifespan, whether it has an effect one way or

the other, it may then be possible to identify the physiological channels through which the gene affects the lifespan. But this is difficult if not impossible if you are dealing with the joint results of a multitude of genes which differentiate two different inbred strains or populations.

Maynard Smith: It will be easier in the mouse, although it will take longer, because you have more idea of what mice die of than I have of what flies die of.

Rockstein: Your results do not really agree with Dr. Maurizio's or mine. The honey-bee lives longer when it has a functioning ovary, certainly in the queenless colony. The housefly lives longer when it is well fed and is laying lots of eggs.

On the other hand, you implied that the effect of temperature in prolonging life was through the destruction of the ovaries. Of course, these occur together and may not necessarily involve cause and effect. Instead, this may be the net effect of temperature through a more important higher level of control, which affects ovary development (as well as other processes) so as to result ultimately in the rapid dying off of the population.

Sacher: There is also the opposite interpretation, that since the ovary is regenerated it is not the destruction, but rather the regeneration, that extends life.

Maynard Smith: You can get the same results with animals which never had and never will have ovaries—these animals will live much longer than their double first cousins who have got ovaries. It is reasonable to take the simple hypothesis that it is the egg-laying that matters. Since, as Prof. Wigglesworth commented earlier, females are liable to suffer from protein-shortage, my results are quite consistent with yours. On sugar and water your females may have died young because they were suffering from serious protein shortage. My experiment suggests that if you deprive a female of her ovary or cause it to regress, then she does not suffer from protein shortage as much as she would if she were laying eggs.

Gerking: Can you give an estimate of the size of the ovary in relation to the body? Is it as much as 50 per cent?

Maynard Smith: I do not know exactly, but it is certainly not as much as that.

Gerking: In the fish I talked about the ovary may weigh as much as 20 or 30 per cent of body weight at maturity. Once the eggs are shed then you can hardly find the ovary. Its restoration to this 20 or 30 per cent level requires a great amount of energy. I wanted to point out that in both the fish and *Drosophila* a very large proportion of metabolism is devoted to egg production. You have concluded

that egg production is at least one factor responsible for ageing in *Drosophila*, but I have been unable to find any relation between fecundity and age in egg-laying fishes.

Hinton: In most flies when the ovaries ripen the abdomen swells greatly, and the ripened ovaries occupy a considerable percentage of the total volume of the abdomen. The other organ systems are frequently much displaced by the ripened ovaries,which may account for a high percentage of the total weight of the female.

Maynard Smith: They are not so big in *Drosophila*. Eggs are pumped through at a rate of about 30 or 40 per day, but the ovary itself is never very large.

Berg: Is the ovary a self-regulatory mechanism in the fly? A selective effect on the ovary without affecting hormonal regulatory mechanisms would be unusual.

Maynard Smith: What do you think the regulatory mechanism might be here? The ovary is not itself a hormone producer, is it?

Wigglesworth: One of the main detectable abnormal effects on the insect of raising the temperature is the effect on hormone action. You can get an insect which is apparently metabolizing normally, but you knock out the action of the growth-promoting hormone. The ovary certainly appears to have a hormonal influence, a sort of feedback influence, upon the endocrine system. So that even in your ovariless insects produced genetically you might be impairing their endocrine system through lack of this feedback mechanism.

Maynard Smith: The ovariless flies are the offspring of females homozygous for the mutant grandchildless, and the suspicion, which is not adequately demonstrated, is that females carrying this gene produce eggs without pole plasm. This would explain the fact that the female offspring have no ovaries and the male offspring no testes. If the ovariless females had lived for a shorter time than the controls, I would have said something else was wrong too, but they lived 50 per cent longer. I was very reluctant to accept this simple mechanical explanation, that they live longer because they do not lay eggs, but everything seemed to fit in so well that until something does not fit, I have to accept it.

Kershaw: The overwhelming effect of ovaries and this relation to nutrition has been shown in some experiments that we have done. We have exactly the opposite results from those in your *Drosophila*. In *Aedes aegypti*, which depends largely on blood meals, the virgin females live for a much shorter time than the normal egg-laying females (Lavoipierre, M. M. J. (1958). *Nature* (*Lond.*), **181**, 1781). This disparity would fit in with the complete dislocation of nutrition invoked by the disturbance of normal ovarian function.

GROUP DISCUSSION

Comfort: I would like to emphasize the variety of the material to which we have been obliged to apply the term lifespan. I am inclined to say that if a single parameter must be used to designate a curve—it is better it should not be, but if it must be—for most of the purposes we have been talking about I would favour the modal age of adult death which Dr. Benjamin showed us.

Unfortunately there are many curves for which you cannot use the modal age of death. In zoo animals there is effectively no mode, since the survival curve is almost an arithmetic straight line (Comfort, A. (1957). *Proc. zool. Soc. Lond.*, **128**, 349; *Ciba Found. Coll. Ageing*, **3**, 14.)

Another possible parameter that has been mentioned is the median. It has the advantage for experimental purposes that you need not wait till the animals studied are all dead—you can rush into print when half of them are dead. But I think its standard error is a little difficult to handle. It also has the drawback that it is very sensitive to the effects of environment on the survival curve. The last decile is far more stable in this respect.

You could also use the limit. The limit has the advantage that even in small populations of animals one or two commonly survive much longer than their fellows—their performance is a better index of "physiological" performance than the crude mean or median. Its drawback is the existence of a large number of doubtful records of very old age in man and animals.

In Bourlière's curves for birds, and also many of Beverton's curves for fish, standing mortality at low ages is so high that it is effectively independent of age; the most obvious parameter is the half-life, but since these populations contain some long-lived individuals the limit is also possible. But they cannot be made to indicate what happens to the mortality at ages which are so rarely reached.

To compare lifespans we might fit a set of curves and compare their time scales. Without using any equations I superimposed those for the K/B *Drosophila*, for a human population (1941 United States males), for Murie's wild sheep, and for my thoroughbred mares, on different time scales, by fitting the last three quartiles of each unsmoothed curve. That is another way of defining and comparing lifespans; but if you do that you must allow for the fact that man has a uniquely long developmental period, whereas sheep have

not, while in *Drosophila* I used only the imaginal lifespan and ignored the whole of its previous larval career.

I have not included among these examples the agricultural type of lifespan, which Dr. Hartwig mentioned for his cattle and horses; that is yet another question. And I should add that in fish kept in the laboratory we obtain a series of curves under different degrees of environmental comfort which are very like those for mammals, including man. In all cases the force of mortality rises with increasing age.

Mühlbock: The mouse has the advantage that there are inbred strains available, as you know, and we use them in our work on cancer research. These inbred strains come from brother-sister matings, made for at least 20 generations, and all the strains I shall refer to here have been through more than 100 inbred generations. Survival curves for the females of the DBA and O20 strains show that hybrids from the two strains live longer than the pure inbred lines. An analysis of the DBA strain shows that the males die first and the virgin females live longest; in between come the breeding females. By breeders we mean females which are allowed to rear their young. For special purposes in cancer research there is another group of females which is described as force-bred. That means that the young are discarded after birth, so that no lactation occurs. The lifespans of the force-bred females are plotted from the 12th month, after the fertility period has ended, so their shorter lifespan cannot be due to accidents in pregnancy and there must be some influences which affect lifespan in the second half of life when the fertility period has ended. The CBA strain is one of the longest-lived strains we have; some of the virgin females live to an age of 35 months. Here again the virgin females have the longest survival. In this strain the males are not so different, but the force-bred females, with rapid pregnancies and without lactation, have a shorter survival. But that is not the case in all the different strains we have. In the O20 strain the differences between the various states are not so great as in the other ones. There are therefore differences in these different strains but I do not know what is the reason for them.

Rockstein: In the life-tables of the male houseflies I was interested particularly in the d_x values because from about the 10th to the 24th day of life this represents a fairly large part of the population. We are really at the peak of the mortality during this period of cohort existence. In the females there is a grouping in the d_x values, so that they reach a peak, then fall a little, and then reach another peak, and so on. This illustrates the idea which the probit curve seems to suggest, namely that the female is involved in a more complicated type

of mortality for the populations, so that at a different age an additional factor seems to be interjected into the mortality picture. Perhaps Mr. Perks would comment on these tables [not printed].

Perks: First, I find it rather strange that you have such a large number of "ages" in your life-tables. We actuaries, of course, string out the rates of mortality for each year of age, but that is for the practical purposes of life assurance. For understanding the mortality that underlies the life-table we would certainly compress it, and we would not have 67 values of the independent variable. We would probably group these in fives and show the values of q_x for five intervals at a time. That is a general question of presentation, and of trying not to confuse the reader with too many figures.

The next point is that the distribution of d_x for male houseflies gave me the impression of a curve very much like the Karl Pearson type 3 frequency curve, that is the gamma distribution, that comes up to a peak fairly quickly and has a long tail away to the right. The mortality curves for electric light bulbs that E. G. Pearson published 25 to 30 years ago had very much of that characteristic; they were fitted fairly well by the type 3 distribution. If we are actually to understand anything about the underlying mathematical processes of mortality curves, we should start with the simpler organisms, or simple physical objects, and electric light bulbs are particularly suitable for this purpose. You can get them fairly homogeneous, and put them on a uniform circuit, so cutting down much of the extraneous variation. It certainly is interesting to see a death curve with a long tail to the right. The human death curve tends to have the tail to the left—coming up slowly to the peak, and then coming down very sharply. Beard has fitted incomplete gamma functions to a number of human life-tables, but he had to do a bit of manipulation with the data first, to remove the accident and infectious diseases mortality, otherwise the tail on the left-hand side would not asymptote to zero. There is a mathematical model that provides some analogy with the death process. Imagine that a population of objects are put on a wall, and shot at at regular intervals so that each is equally likely to be hit. Then suppose you define death as when a particular object has been hit n times; then the death distribution is in fact the type 3 distribution. Thinking along those lines may help us to get mathematical representations of the death curves of more complicated objects. I am particularly interested to see that the housefly appears to give a relatively simple distribution.

My impression of the female table is that it is rather similar to the male, except that the peak is much flatter. So far as the so-called

subsidiary peaks are concerned, I would be astonished if they were not just the result of random error. q_x is irregular, and so obviously no graduation process has been applied. I assume that the life-table was obtained by following the history of a cohort, and that the l_x figures are in effect the numbers actually surviving to each age, the numbers being reduced to a radix of a thousand.

Rockstein: That is right. There were about 4,000 animals of each sex there, 3,875 females and slightly more males.

Perks: That is a technique that with humans we have not found very helpful, because it takes 100 years to follow a cohort through. But even though you get your rates of mortality that way, before I would draw any conclusions whatever from bumps on the d_x curve I should want to put a light graduation through the q_x values, and then recompute the l_x and d_x columns. You would have to apply a goodness of fit test. But a quite elementary graphical graduation would probably be sufficient to get rid of the accidental bumps in the d_x column.

Gerking: What do you mean by a light graduation?

Perks: I mean putting a smooth curve through the points represented by q_x, so that you get rid of, or greatly reduce, the random errors—on the hypothesis that if you had a much larger number in your sample the departures from the smooth curve would largely disappear. I agree that the assumption of the smooth curve for the q_x is only a hypothesis, but there is a great deal of observational evidence for that assumption, provided you keep your condition reasonably constant.

Sacher: When you say smooth, you do not necessarily mean simple?

Perks: No. There is no satisfactory mathematical definition of smoothness. There has been some controversy in the Institute of Actuaries on what we mean by smoothness, and some people suggest it should be absence of roughness!

Rotblat: How sensitive is the gamma distribution to the value of n?

Perks: You can get a wide range of different curves with different values for n.

Comfort: I am impressed with that remark, because this is almost what Failla or Szilard have suggested is in fact happening, isn't it? (Failla, A. (1958). Proc. Ageing Conf., Gatlinburg. Washington, D.C.: A.I.B.S., in press. Szilard, L. (1959). *Proc. nat. Acad. Sci. (Wash.)*, **45**, 30). The objects are actually being shot at by radiation, and this may be one of the causes of chromosome deterioration.

Perks: If you are interested in that, R. E. Beard developed the subject further some years ago (see Appendix, p. 302). If you increase

the probability of being hit according to the number of times the object has been hit before, and if you proceed further and increase the speed of the shooting, the mathematics develop in the direction of the Makeham curve and certain modifications of it.

Maynard Smith: I do not believe for one moment that the shape of these curves has anything to do with the organism that has been studied. I think it has something to do with the environment in which it was studied.

Perks: I have thought about this problem for a long time and I believe the shape has something to do with time.

Tanner: You would expect a different-shaped curve in a less long-lived organism?

Perks: No, I think it is the cumulative factor in life; injuries and so on are additive, or cumulative in almost a geometrical sense, and you must expect to have exponentials coming into the form of the mortality rates.

Tanner: Does this make the change, then, from the gamma function into the Makeham type of curve? You think that the reception state changes according to the number of shots impinging?

Perks: Yes.

Holt: In the models for fitting the depreciation of motor cars death is assumed to result from either single big accidents, or an accumulation of small ones, and a complex death curve follows; it seems to have some possible application to animal mortality.

Rotblat: I am concerned to know what lifespan is because we have to express some of our findings in terms of lifespan. For example, people often speak about the effect of radiation in causing a shortening of the span of life and they put down figures of the percentage of life-shortening per röntgen. But everyone I have asked what he meant by the term lifespan gave a different answer. I was hoping that perhaps in this meeting we might come to some agreement on that. I was impressed by your remarks on the first day, Dr. Benjamin, when you brought in what you called the senescence peak. This peak seems to me to be the quantity to put down as the "normal lifespan". I was particularly interested to see data presented by various people which showed that although the shapes of the mortality curves may differ enormously, nevertheless for a given species they all reach nearly the same end-point. If we could draw the ideal curve, i.e. if we could eliminate all deaths due to accidents, infections, etc., then the "normal lifespan" would be obtained immediately from the senescence peak. But in practice this will be very difficult, because most mortality curves do not approximate to this ideal. We are, therefore, still left with the question of what we

mean by lifespan. If one could establish, once and for all, the normal lifespan for a given species, then the observed mortality curve would tell us the deviation due to environmental conditions, such as being kept in a zoo, or hunted. Then we might introduce another index to take these conditions into account. We could take the 50 per cent survival time from the actual mortality curve and the ratio of this to the normal lifespan might serve as an index of, say, longevity or senescence. These two quantities, the normal lifespan and the 50 per cent survival time, might be the proper parameters to use.

Comfort: The limit, as I say, is not always advantageous, because of the very great divergence in the reports of maximum age in animals. My own feeling is that once you can get a family of curves like this, or a rough indication of the family, you could perhaps take a point 10 per cent back from the limit.

Rotblat: If you take the mortality curve, then depending on the condition in which the animals are kept we would obtain different times for the 50 per cent survival but the same limit.

Comfort: I am thinking of cases where you have not got curves as good as that. If you do have such a family of curves, there is no difficulty. The trouble is to know what to do with the sort of thing that Sacher was describing, where he wants to compare a whole range of mammals; merely to get a rough correlation it is necessary to give some sort of figure which one can compare.

Perks: The difficulty with the modal value is that it is influenced to a certain extent by the infantile mortality, and by mortality from accidents and infections. If you reduced those mortalities, then, as a mere piece of arithmetic, the mode is advanced and the curve of death becomes much steeper, by the mere fact that more lives survive to the ages at which the rates of mortality are high. I have been thinking about this question of what would be a useful measure of lifespan. Some sort of technique such as actuaries use, which we call multiple decrement technique, might be used, at least in theory. It is rather laborious, but if you could separate from the death curve all those deaths which have nothing to do with lifespan—accidental, predatory, infantile, and anticipatory deaths,—then there is a technique for getting a residual life-table, a hypothetical life-table, that is concerned only with those causes of death which affect biological lifespan. This would have all the disturbances taken out of it, and of course you would get a much later and taller death curve.

Comfort: The trouble with that is to know which causes are age-dependent.

Rockstein: I think we are being unrealistic about this. I would suggest that mean longevity seems to be a thing that you could

obtain all the time, regardless of the cause of death. If you are concerned with a standard value or reference against which you can compare, why not use an animal, as you do in the laboratory, from which you can get such data? I have been amazed that for over ten generations in the housefly, for example, one can continue to get the same mean value. I say this value is a good basis for comparison in an experimental study. With the white rat, under specific laboratory conditions, for example, the only thing that will vary in irradiation tests will be the extent or dosage of radiation. With humans we run into another problem because we always deal with life expectation based on a population that is not always an identical cohort, but for experimental studies we can get cohorts of an identical nature for inbred lines of a number of species of lower animals. I do not see why the mean longevity is not as good a criterion as anything else; it considers the accidental deaths, it considers the possible disturbance that the mode would have from having had early deaths or accidental deaths, and even a tail at the end resulting from the extended longevity of the few long-lived cohort members.

Perks: I am sure you are right for your problem, but different problems require different solutions.

Rotblat: If we say, for example, that radiation causes a contraction of the scale of life, and suppose we are dealing with the ideal case in which all animals die of old age, then for the irradiated animals we would obtain the same curve but bodily shifted to the left. This would be very nice, but in practice it may not be so. It may be that radiation has caused earlier deaths without changing the end-point. The curve would then change completely. Which of these will actually happen depends upon the effect that radiations have on the lifespan.

Sacher: The average is certainly the first quantity to use in the experimental situation, but you cannot characterize all the effects of radiations, or of any other environmental influence, in terms of a single parameter. Empirically you can then proceed to the succeeding central moments. The question is to find out what parameters of the survival curve are being influenced by the particular environmental factors under investigation. I have pointed out how, in studies of radiation effects on mice, you could characterize the effects of radiations in terms of the A and the α parameter of the Gompertz equation [$q_x = Ae^{\alpha x}$]. A single dose of radiation—to restate what I said yesterday—causes a change in A, without a change in α. Continuous exposure causes a change in the α coefficient. It is perfectly true that this Gompertz equation is not an entirely adequate description of the life-tables of natural populations, but it should be

borne in mind that this is an oversimplified form, suitable for discussing general principles. In application to data, more complicated expressions are used. Each major disease category needs a separate Gompertz term, as has been shown by Simms (1940. *Science*, **91**, 7). In addition the experiment need not be simply proportional to age, x, but may be a function of x. Thus the general expression for the description of mortality in terms of a summation of Gompertz terms is

$$q_x = \sum_{i=1}^{n} A_i e^{f_i(x)}$$

Perks: If you are fitting mathematical expressions to your data of statistical distribution, then clearly you estimate the parameters, and your estimated values for the parameters sum up the statistics. I thought the problem we were really talking about was how to characterize statistics for which you have not got a mathematical expression. For a single measure to be sufficient the distribution would have to be a very simple one, such as $l_x =$ an exponential, in which case you have got a single parameter and the measure might be the constant rate of mortality or the half-life. In any other case, you cannot sum up the distribution by a single measure, and you cannot even say that any particular measure is the best one. All you can say is that for some purposes one measure may be better than another. You have to accept that the expectation of life or the half-life or mode or whatever you may regard as the lifespan, gives you only part of the information contained in the statistics.

When the life-tables of different animals are compared, it may be that the lifespan is good enough, and I think that view was expressed yesterday. When the mortalities of the same species in different environments are compared, I would agree that expectation of life is probably as good as any. In general terms, if you are going to have more than one figure as a measure of a death curve, probably the 1st, 2nd, and 3rd moments of the death curve would be as good as any. It is not until you get a mathematical expression for the death curve that you can really say that any parameters are better estimators than any others.

Benjamin: All this discussion of lifespan seems to be only a means to an end; we really want to get away from lifespans to considering the ageing effects, for example, of changes in environment. For that we really want two things. First, we need some kind of function which is as discriminating as possible of the effects of ageing, so that it is very sensitive. That suggests that what is wanted is the middle part of the survival curve where a small change in the survival risk

may make a difference between the curve bulging up one way, or bulging down the other. The largest possible dispersion of effects is found here, which brings us to the idea of the 50 per cent survival age point. To get a time scale which enables comparisons to be made between different kinds of animals, on the other hand, you need something which is not sensitive to that kind of change. This suggests that you should use the peak of the curve of deaths, because although the height of the peak is very much correlated with anticipated deaths and so on, the actual movement of the peak is not particularly sensitive. So while it is unprofitable to talk about an ideal lifespan, it is quite practical and profitable to look at large families of curves of death for the same species, and see what kind of shape they tend to in general, so that you can get for the different species a typical modal attained length of life, which you could use as the time scale.

Comfort: This is Bodenheimer's "physiological longevity" (Bodenheimer, F. S. (1938). Problems of animal ecology. Oxford University Press).

Perks: I would like to plead that you should all take an interest in the international actuarial notation. I think it is a very good thing that all scientists should use the same notation if there is one which is generally accepted. Dr. Benjamin has included some of it in his paper and I think it probably could be extended to cover all your needs.

We have heard the phrases lifespan and ageing over and over again but I do not think you will ever succeed in rigorously defining them. I think they are best left as rather vague concepts, as we know in general what we are talking about.

I have been a little puzzled by the extent to which logs have been taken of various observed figures. To me it only confuses the issues, particularly when you have a graph on a logarithmic scale, although I do understand that sometimes it is necessary to do that to compress the graph to reasonable dimensions. But there is no excuse for taking logs in arithmetic merely to get rid of some of the variations, and apparently to produce a correlation or regression which possibly is not there if you do not take logs. What does the logarithm of a residual mean? When you take a logarithm of the cephalization index and then associate it with a logarithm of body weight, and finish up with a logarithm of a lifespan, what does it all mean?

There may be a very simple technique that might be useful for those of you who study lifespans or mortality of animals in their natural state. I understand that it is very difficult to get their ages, but often I imagine you will find stationary populations in the natural

state. So if you take the crude death rate over an interval of time, then a fair measure of the expectation of life, in terms of that interval, is the reciprocal of the crude death rate, provided that population is stationary, or nearly stationary. If it is not nearly stationary, you can probably make an approximate adjustment.

The only other thing I want to say is that the actuary's use of life-tables is very different from yours. The life-table is not an end in itself for actuaries; it is merely a step on the way from a set of mortality rates to the calculation of premium rates, reserves, bonuses and surrender values.

Sacher: Logarithms are not introduced to mystify. They are actually a great convenience for computation. The classical law of allometry is that one dimension of an organism is related to another as $[Y = AX^k]$ so that one of them varies as a power of the other; these allometric relations are almost always presented graphically on a double logarithmic scale. When you take the log of Y and the log of X there is then a linear relationship between these values. There are great advantages in using logarithms to fit a power function by least squares. All of these considerations apply to brain weight, body weight, and lifespan as I have analysed them here. The index of cephalization is a pure number. It is the logarithm of the ratio of the actual brain weight of a species to the brain weight that is predicted by the overall regression of log brain weight on log body weight.

Logarithms are also convenient in the present application because they introduce the property that all of the observations have approximately the same statistical weight in terms of the logarithmic transform. The lifespan, brain weight and body weight measurement all have about the same percentage error from mice to elephants and therefore the error in logarithmic units is roughly constant, even though the original absolute values have a million-fold range of variation—from 5 grams or so to 5,000 kilograms.

Perks: I agree that if you have reason for a relationship of that form, then logarithms may ease the arithmetical processes.

Sacher: There is no reason, in the sense of a general theory of growth and of the relationship between parts of an organism, that is capable of explaining why the allometric relationships should be of this form. It is, however, a fact of observation that the power function does describe these relations, and no other function does it as well.

Comfort: It is also true that in drawing the survival curves of birds and small mammals, where over a large part of their lifespan their mortality is so high that it is almost age-independent, most people

use an arith./log scale, arith. for time and log for survival, so that constant mortality gives a straight line.

Tanner: I have been sitting here for the last half-hour with a very strong feeling of *déjà vu*. The people who are interested in growth have been fitting growth curves with decreasing enthusiasm for about 35 or 40 years. It seems to me that you are pursuing a vertiginous and descending pathway!

I do not think there is anything in the general aspects of growth which leads one to suppose that the allometric relationship is very useful in general. There may be instances where it is necessary, not from any theoretical considerations but because using logs produces a straight line; I do not think that there can be any other justification.

Sacher: A transformation, such as the logarithmic, cannot increase the amount of information contained in a set of data, so if the correlation of the transformed variables is $0 \cdot 99+$ this expresses a fact about the data, i.e. that only a fraction of a percentage of the total variance is error variance when the proper functional relation between the variables is found. No *a priori* justification is needed for the use of the power function. In my own and Brody's data there is no question about its appropriateness. The fact that some other data are adequately rectified by a linear plot is interesting but it cannot contravene the allometric relations as they have been established in many other cases.

Chitty: My particular problem is to find out why animal populations in nature do not go on increasing indefinitely, and what it is that they die of. Most people up to the present have considered that deaths in nature could be almost entirely accounted for through predation or epidemic disease, heavy infestation with parasites, or food shortage, but it is now clear that this is a wholly inadequate explanation, particularly for the huge mortalities which occur in the young stages. The problem arises—what exactly is it that they die of? The suggestion was first made by P. H. Leslie and R. M. Ranson in 1940 (*J. Anim. Ecol.*, **9**, 27), for the field mouse, that the life-table type of explanation might be applied to field populations. In the laboratory you recognize that, with age, there is an increasing probability of death from a variety of causes which are peculiar to the particular environments—that is to say a group of mice in one laboratory would not have the same final causes of death as they would in another—but in each case there would be the common fact that as they grew older they became increasingly liable to die of whatever it was that was peculiar to those environments. The field evidence strongly suggests that this may be a profitable way of

looking at natural populations, too. The problem now becomes to try and find some general law which is applicable in spite of the fantastic variety of conditions in the field. I think one would never hope to find any common causes of death associated with the actual time of death in nature. Every environment differs in its hazards from every other one. The point is, can we find anything in the properties of the animals which does obey some sort of general law under all these varied circumstances? In other words, what is it that makes an animal increasingly likely to die regardless of what actually kills it in the end? We might divide the problem into both multiple and single processes. The final causes of death would be the multiple processes, and there we have very little hope of introducing much unity; but by concentrating on susceptibility there may be some hope of finding a common process which can equally well be studied in those animals which live to a great age in the laboratory, and those which die at a much younger age in nature. Exactly how one goes about this I do not know, and that is the point at which my work is hung up. I have to account for very violent changes in the probability of survival at different times of the population cycle, and exactly where does one go to look in the organism for something which may be an index of this change in properties? That seems to me to be very similar to the problems with which one is faced in trying to account for the increasing probability of death with age. Animals in the field very seldom live to an age at which you can say they are senescent. Nevertheless, it is a fact that even at a much younger age than they die at in captivity, some species periodically show this very great increase in probability of dying (see Green, R. G. and Evans, C. A. (1940). *J. Wildlife Mgmt*, 4, 220, 267, 347). The question arises of whether or not we should regard these as problems of senescence and ageing, or as much more analogous to the high probability of human beings dying young, or whether age is irrelevant and some index of physiological condition is the only thing worth trying to find in any species.

Tanner: There does not seem to me to be any connexion between the situation in non-domesticated animals and the situation in the human. All the other mammals and birds would have died early in terms of human growth. The human was the only animal which seemed to be surviving long enough to experience senescent processes. Cellular ageing might paradoxically have been closer to the situation in man, than is the situation in the passerine, for example. After what Dr. Chitty has said I feel like withdrawing this comment, because if in other species the probability of their dying in the field increases with age, this is the fundamental thing. It comes back to

what I was trying to say before, that just as in growth we talk about developmental age, so we can talk about the probability of death in any given situation as developmental age further down the scale. If that is really true, if these analogies can be made the same in animals and man, then we can use the results of both field workers and the experimentalists much more usefully to shed light on the human situation.

Comfort: The figures we get for small mammals have often misled people into thinking that all mammals behave in this way. We have only very few figures for the larger ones but there is some evidence that many larger mammals in the wild achieve high ages quite often. I would be very surprised if some of the larger wild ungulates didn't live long enough to senesce. Wild horses, if one had the chance of observing them, may perhaps live to a fair proportion of the age reached by tame horses.

Sacher: Porcupines can survive until they are so arthritic they can hardly climb trees—nobody comes up against them except mountain lions.

Verzár: Dr. Chitty, did you imply that the time of survival for a certain species depends on the number of individuals living at the time? If you put a pair of fish in a pond, they will have certain survival characteristics for their age. When the pond becomes full with fish the population will become constant. Then the individual survival curve will probably be different, otherwise the number of fish would continue to increase, which is impossible because there is not enough food.

Chitty: The number alive has a very great influence on the survival rate but the survival time can certainly not be predicted from the numbers of the animals alone. One must also take into account the behaviour of the population; experimentally you can have a family group of 50 animals which is perfectly amicable and has a good survival rate, yet with two animals in a similar space who are strangers, the survival time of one of them will be about half a day. The presence of other hostile animals of the same sort is, I think, one of the strongest environmental factors which does affect survival, regardless of the amount of food available.

* * * *

Danielli: I shall not attempt in any way to summarize this meeting. I have been considerably refreshed by it in many ways. We have learned, for example, that man, skunks and porcupines are amongst the few animals who know how to survive into the period of

senescence. The nature of this grouping probably has some moral significance.

A point that impressed me very much was the difficulty of evaluating the significance of data obtained from animals in captivity, which are living in conditions of constant diet, no exercise, constant illumination, very little in the way of seasonal change, and so on, to which even animals which have been selected for laboratory purposes are not really 100 per cent adapted. After all, the period of adaptation to laboratory life is comparatively short compared with the period of evolution. I do not really know what can be done about that. What is outstandingly important is that, wherever possible, a pathologist should look at the animals when dead, and this should be done for insects as much as for any other form of animal life.

The concept of a biological time scale continues to interest us, though it is obviously even vaguer than some of the other concepts, which, as Mr. Perks remarked, are better kept vague. However, this particular one is of no use to us unless we can measure it. It is useless to continue to use it without exact definition.

Whatever the source, if we exclude accidents to which the individual concerned does not contribute, in most instances susceptibility to mortality in a species or a strain does develop in a typical manner. It is perfectly clear from what has been said that if one cause of mortality is removed, for most of the animals for which we have had data analysed in sufficient detail here, some other cause of mortality would rapidly cause life to come to an end in the individuals which have survived. The total gain of lifespan which would result from eliminating one cause of death is not great. In other words, operationally we *appear* to be dealing with a unitary process. Whether ageing is in fact unitary, however, cannot be determined from the data we have been presented with so far. I am not at all clear to what extent Maynard Smith's theory of synchronization of independent lethal processes is a valid one, but it is, I am sure, a very important matter indeed to have had raised, and one which necessitates a good deal of further thought and investigation.

The concept of a limit to the life of a tissue which is set in terms of the energy conversion per unit mass per life cycle is a very attractive one, but possibly dangerously attractive. If we accept it at its face value, it presumably means that living matter commits accidents at a rate which is proportional to the rate of energy conversion in it; this is quite a tenable view physically, and one which must surely be open to investigation. We need more data, for example from the study of hibernating animals, and from the use of metabolic poisons. We ought to use metabolic poisons and radiation in attempts to

desynchronize some of the processes which may be synchronized. It may be in this connexion that we could make some progress by studying systems in which one is normally dealing with symbiosis. Here the breaking-up of the symbiotic relationship might reveal phenomena which would be difficult to reveal by any other method.

A cellular approach to ageing would under certain circumstances facilitate examination of the actual process of ageing, if this is in fact to some degree unitary, but I am not convinced that this is so with higher animals. The ageing process in higher animals may be fundamentally a function of the complex of cells and operate at a higher level of organization than is present in cells.

Another point which we have not discussed yet, but which we are probably all agreed upon, is that it is quite possible that lifespan in man, as we see it now, is an entirely accidental by-product of selection for breeding efficiently at a much earlier age, and does not in any sense correspond to social needs of the moment. An accumulation of experience has become much more important, or at any rate equally as important as physical vigour; therefore socially speaking there is a very good case for anything which will enable us to modify the expectation of life in a radical manner. Looking at this from the long-term point of view, I think the possibilities for so doing would in fact be good by chemical means, provided ageing does in fact occur by a unitary process. If on the other hand it is due to a very large number of non-unitary processes which do not have any common mechanism, then I think the chemical approach to extension of lifespan is fraught with so many difficulties that it is hardly worth considering. To illustrate the order of magnitude which I would expect if there is a unitary process involved, I would like to refer briefly to the rate of mutation, or rather the rate at which damage is caused by radiation. It is of course a tenable hypothesis that somatic mutation is, one way or another, directly concerned with the ageing process. There are cells which are killed by a dosage of the order of 100 r.; there are other cells which require a dosage of 1,000,000 r. to kill them. This difference of four orders of magnitude is not at present, as far as I know, accountable for in any cytological or physiological terms whatever. Therefore, if ageing were associated primarily with somatic mutation, or some other generalized mechanism of this type, we might expect that under suitable conditions lifespans could be varied by that order of magnitude. This sounds a little like science fiction, but all of us have seen so much of what we regarded as science fiction 20 years ago turning up as reality, that I think we must envisage the possibility that we may be able to make radical changes in lifespan.

My final comment is that I regard it as singularly unfortunate that so much of the research on cancer is conducted essentially without reference to the phenomena of ageing, of which I think it is a part. I believe that not only would a study of ageing benefit from more knowledge of what is going on in older animals, but the whole field of investigation of cancer might benefit equally, and perhaps far more. This for the simple reason that to a very considerable degree, at the moment, cancer experiments are conducted by putting transplantable tumours into young, often rapidly growing animals, and then seeing what could be done in the way of chemotherapy in these conditions—a thing which does not approximate very closely to what happens in the average human patient. Prof. Mühlbock's laboratory is a shining example of an institute where this isolation of cancer research from ageing research does not occur, but I hope it will not long continue to be one of the very few shining examples.

APPENDIX

NOTE ON SOME MATHEMATICAL MORTALITY MODELS

R. E. Beard

Pearl Assurance Co. Ltd., London

1. A satisfying basis for a law of mortality would be a formula that, starting from some fundamental concepts about the biological ageing process, led to a distribution of deaths by age which was comparable with observational data. Such comparison would not be simple and straightforward because environmental and secular factors would introduce distortions as compared with the theoretical underlying distribution.

2. In the course of numerical work, extending over a number of years, on the expression of human mortality functions by mathematical formulae, various attempts have been made by the writer to develop an approach on this basis. The results obtained have not led to any satisfying formulae, but they are suggestive of different lines of approach and have been summarized below in the hope they may be of value to others interested in the subject. The note follows the sequence in which the ideas have developed in the mind of the writer and leads from considerations based on the force of mortality, μ_x, to those based on the curve of deaths, $\mu_x l_x$.

3. The first mathematical expression which provided a reasonable representation of the observed force of mortality in human data was that first proposed by Gompertz (1825) and later modified by Makeham (1867). Basically the "law" was derived by postulating a relationship between the rate of change of the force of mortality at any age and its value at that age. The next significant modification to the Makeham law was the system of curves devised by Perks in 1932 and of which the important formula was the logistic. Many human life-tables have been graduated by this basic curve, modified in some instances to allow for special features of the data, particularly at the younger and early middle ages, and the clear fact emerges that adult human mortality can be very well represented by a logistic curve of the form

$$\mu_x - A = B\, e^{\lambda x}/(1+D\, e^{\lambda x}) \qquad (1)$$

which will be referred to as a Perks curve since this is the name by which it is generally known by actuaries (Perks, 1932; Beard, 1936, 1939*a*, 1951*a*, 1952*a*; Registrar General, 1951; Mortality of Assured Lives, 1956).

4. Now μ_x is the ratio of the ordinate at age x of the curve of deaths to the area under the curve above age x. We may look upon the curve of deaths as a frequency distribution of deaths by age at death and for many types of frequency curves it will be found that this ratio has a sigmoid form. It is not apparent whether the satisfactory representation of μ_x by a Perks curve is because the formula has a theoretical significance or because the formula does provide a good approximation to the particular function of a family of frequency curves which can be used to represent the distribution of deaths by age (Perks, 1953).

5. What evidence is available tends to support the idea that the force of mortality does not continue to increase indefinitely with age. The concept of a limiting age by which all individuals must be dead (i.e. a maximum lifespan) does not seem to be in accordance with the facts—the use of a limiting age as a mathematical device to cut off a long slender tail has nothing to do with the present discussion. Formula (1) leads to an upper limit of B/D for μ_x and it is not without interest to note that the numerical values of B/D obtained from the graduation of human mortality data are of the same order as the force of mortality which can be deduced from select mortality tables as being appropriate to "damaged lives", i.e. about 0·57 (Beard, 1951*b*).

6. If the rapidly decreasing mortality associated with the infantile and growth period be ignored the pattern of human mortality then exhibits a basic sigmoid form on which are superimposed waves and other disturbances. The waves appear to be due largely to secular effects (e.g. selective effect of war deaths); the main disturbances are those arising from accidental deaths and the (rapidly disappearing) hump at the early adult ages from deaths from tuberculosis.

7. For a broad mathematical approach we will be concerned with (a) accidental deaths (assumed to be at a constant rate at all ages), (b) an upper limit to the rate of mortality, and (c) a progression in time.

Gompertz' law arises by using condition (c) only,

$$\text{i.e.} \quad d\mu_x/dx = \lambda\mu_x \qquad \text{whence} \quad \mu_x = B\,e^{\lambda x} \tag{2}$$

Makeham's law arises by using conditions (a) and (c),

$$\text{i.e.} \quad d\mu_x/dx = \lambda(\mu_x - A) \qquad \text{whence} \quad \mu_x = A + B\,e^{\lambda x} \tag{3}$$

Perks' law arises by using conditions (a), (b) and (c),

$$\text{i.e.} \quad d\mu_x/dx = \lambda(\mu_x - A)(E - \mu_x)/(E - A)$$

$$\text{whence} \quad \mu_x = A + \frac{(E-A)\,D\,e^{\lambda x}}{1 + D\,e^{\lambda x}} \tag{4}$$

The Perks (logistic) relation can be expressed as stating that the rate of change of μ_x is proportional to the product of its value and the amount by which it falls short of its upper limiting value.

8. If the requirement of a constant upper limit for the rate of mortality is relaxed other formulae can be developed on similar lines to those of the preceding paragraph. For example,

$$\frac{d\mu_x}{dx} = \frac{\lambda(\mu_x - A)}{1 + B(\mu_x - A)} \quad \text{gives} \quad w_x\, e^{w_x} = C\, e^{\lambda x}$$

$$\text{where} \quad w_x = B(\mu_x - A) \tag{5}$$

and

$$\frac{d\mu_x}{dx} = \frac{\lambda(\mu_x - A)\left(1 + \frac{D}{B}\overline{\mu_x - A}\right)}{\left(1 + \frac{2D}{B}\overline{\mu_x - A}\right)}$$

$$\text{gives} \quad \mu_x = A + \frac{B}{2D}\left(-1 + \sqrt{1 + 4\,D e^{\lambda x}}\right) \tag{6}$$

Formula (6) is equivalent to a continued fraction form for μ_x, i.e.

$$A + \cfrac{B\,e^{\lambda x}}{1 + \cfrac{D\,e^{\lambda x}}{1 + \ldots}}$$

and the relationship between formulae (2) to (6) is clearly seen by expanding the expressions for μ_x in terms of powers of $e^{\lambda x}$, i.e.

formula (2) gives $B\,e^{\lambda x}$

,, (3) ,, $A + B\,e^{\lambda x}$

,, (4) ,, $A + B\,e^{\lambda x} - BD\,e^{2\lambda x} + BD^2\,e^{3\lambda x} - \cdots$

,, (5) ,, $A + B\,e^{\lambda x} - BD\,e^{2\lambda x} + \frac{3}{2}BD^2\,e^{3\lambda x} - \cdots$

,, (6) ,, $A + B\,e^{\lambda x} - BD\,e^{2\lambda x} + 2BD^2\,e^{3\lambda x} - \cdots$

9. The differences between formulae (4), (5) and (6) will become apparent only at the old or very old ages and unless the data were extensive the differences would be unlikely to be significant for many numerical processes. From a scientific point of view the models are, of course, quite different.

10. An alternative approach to the question, but still based upon rates of mortality, is to determine the conditions necessary for μ_x to be a Perks (logistic) curve, given that the population can be stratified according to a longevity factor and that the basic mortality law is Makeham in form (Beard, 1952*b*). Thus let μ_k^s be the force of mortality at time ($\equiv$ age) k for the group having longevity factor s and let $\phi(s)\,ds$ be the proportion of the initial population having factor s. Then the survivors of $\phi(s)\,ds$ at time k are

$$\phi(s)\,ds.\,\exp\left(-\int_0^k \mu_t^s\,dt\right) \tag{7}$$

and the total survivors at time k

$$l_k = \int \phi(s)\,\exp\left(-\int_0^k \mu_t^s\,dt\right)ds \tag{8}$$

where the integral is taken over the whole range of s.
The force of mortality at time k ($= -d\,\log\,l_k/dk$) is then

$$\mu_k = \frac{\int \phi(s)\,\mu_k^s \exp\left(-\int_0^k \mu_t^s\,dt\right)\,ds}{\int \phi(s)\,\exp\left(-\int_0^k \mu_t^s\,dt\right)\,ds} \tag{9}$$

11. From formula (9) it will be noted that μ_k is a weighted mean of μ_k^s ($= \mu_k^{\bar{s}}$ say). Since the number of lives with heavier mortality will diminish more rapidly than those with lighter mortality, $\bar{s}$ will decrease with increasing k. If the basic mortality is Makeham in form, then $d\mu_k/dk$ will show a slackening off at the higher ages, i.e. the sigmoid feature shown by a logistic curve. In order to meet practical conditions some limitations are necessary on the form of $\phi(s)$; the lower limit must be $\geqslant 0$, but the upper limit can be ∞.

12. If it be assumed that $\phi(s)$ is a gamma function such that $\phi(s)\,ds = ks^p\,e^{-\gamma s}\,ds$ $(0 \leqslant s < \infty)$ and that the mortality function for $\phi(s)$ is $\mu_k^s = \alpha + \beta s\,e^{\lambda k}$, we have

$$\mu_k = \frac{\int_0^\infty ks^p\,e^{-\gamma s}(\alpha+\beta s\,e^{\lambda k})\,\exp\left(-\int_0^k (\alpha+\beta s\,e^{\lambda t})\,dt\right)\,ds}{\int_0^\infty ks^p\,e^{-\gamma s}\,\exp\left(-\int_0^k (\alpha+\beta s\,e^{\lambda t})\,dt\right)\,ds} \tag{10}$$

which reduces to

$$\mu_k = \alpha + \frac{(p+1)\beta\lambda\, e^{\lambda k}}{(\gamma\lambda-\beta)+\beta\, e^{\lambda k}} \tag{11}$$

which is a Perks (logistic) form.

13. The results of the immediately preceding paragraphs are interesting in that the limiting value of μ_k arises from the manner in which the "mixed" population runs off. They have a certain appeal in that they are based on the assumption that the population is not homogeneous in regard to a mortality (or longevity) factor and that the mortality for an individual group continues to increase indefinitely. The limiting value of $\mu_k - \alpha$ as $k \to \infty$ from formula (11) is $(p+1)\lambda = 4\lambda/\beta_1$ where β_1 is the Pearson moment function of $\phi(s)$. For human lives $\mu_x \sim 0{\cdot}6$ at the limit, according to one fairly recent mortality table, and $\lambda \sim 0{\cdot}1$ so that $\beta_1 \sim 0{\cdot}67$, i.e. a skew distribution with a tail towards the higher values of s. If s is a heredity factor, then stability of $\phi(s)$ over generations would imply fertility rates negatively correlated with longevity, otherwise the shorter reproductive period of those with higher values of s would lead to a falling average value of s in the population. It is an interesting coincidence that the distribution of married women according to number of children born has a β_1 coefficient of the order of $0{\cdot}7$ (Papers of Royal Commission on Population, 1950).

14. The assumption of other forms for $\phi(s)$ in formula (9) leads to other forms for μ_x which can have the appropriate shape but which are not convenient mathematically, and no experiments have been made in this direction.

15. From the point of view put forward in paragraph 1 formula (10) suffers from the objection that it is based on the assumption of a Makeham law, and is thus basically empirical. A further approach to the question is to build up models based on the so-called "shot hypothesis" in which individuals are assumed to be subject to random firings and are assumed to die when they have been "hit" a specified number of times. Two main types of model have been investigated, which are referred to below as the "forward" and "backward" models respectively. In the forward model hits are assumed to accumulate and death to occur when the total reaches a certain figure. In the backward model the individual is assumed to start with a quota of units which are progressively lost in time, death occurring when the total remaining falls below a certain figure.

16. The simplest forward model is derived by assuming that the

chance that an individual is hit in an interval dt is p; this leads to a difference-differential equation

$$\frac{dl_t^\alpha}{dt} = -pl_t^\alpha + pl_t^{\alpha-1} \tag{12}$$

where l_t^α represents the number at time t who have been "hit" α times. If l_o is the number of individuals at time o then a solution of equation (12) is

$$l_t^\alpha = l_o e^{-pt}(pt)^\alpha/\alpha! \tag{13}$$

If the number of hits causing death is r, then the survivors at time t are

$$l_t = l_o e^{-pt}\{1+(pt)/1!+ \ldots +(pt)^{r-1}/(r-1)!\}$$

and the deaths in the interval t to $t+dt$

$$\mu_t l_t = l_o e^{-pt} p^r t^{r-1}/(r-1)! \tag{14}$$

The force of mortality at time t is

$$\mu_t = \frac{p^r t^{r-1}}{(r-1)!}\Big/\left\{1+\frac{pt}{1!}\cdots+\frac{(pt)^{r-1}}{(r-1)!}\right\}$$

$$= pe^{-pt}(pt)^{r-1}\Big/\int_{pt}^{\infty} e^{-x}x^{r-1}\,dx \tag{15}$$

Formula (15) shows that the curve of deaths is an incomplete gamma function, or a Pearson type III curve. μ_t has the value 0 for $t=0$ and asymptotes to a value p at $t=\infty$ (Beard, 1939*b*).

17. A more natural function than μ_x in the present context is to use the function which bears the same relationship to $\mu_x l_x$ as μ_x does to l_x, i.e.

$$\frac{d(\log \mu_t l_t)}{dt} = \frac{1}{\mu_t}\frac{d\mu_t}{dt} - \mu$$

and from formula (14) we find this to be

$$\frac{d(\log \mu_t l_t)}{dt} = -p + \frac{r-1}{t} \tag{16}$$

18. Attempts to use the formula of paragraph 16 on human mortality data have been unsuccessful, the shape of $d(\log \mu_t l_t)/dt$ not

fitting well to observed values which show a negative second differential coefficient over the adult ages.

19. As an extension of formula (12) a model can be set up in which the "hits" in an interval can be single, double, etc., in known proportions. The basic relation then takes the form

$$\frac{dl_t^\alpha}{dt} = -pl_t^\alpha + p\sum_{r=1} f(r)\, l_t^{\alpha-r} \tag{17}$$

This can be integrated to

$$l_t^\alpha = e^{-pt}\int pe^{pt}\sum f(r)\, l_t^{\alpha-r}\, dt \tag{18}$$

and by noting that $l_t^o = e^{-pt}l_o$ values of l_t^α can be obtained by successive integration. No experiments have been made using this form, mainly because the form of $d(\log \mu_t l_t)/dt$ seems to be unsuitable for human data. The form of $f(r)$ is also speculative.

20. A different forward model can be devised in which the probability of a "hit" is dependent on the number of "hits" recorded already. We then have the following

$$\frac{dl_t^\alpha}{dt} = -(\beta+p\alpha)\, l_t^\alpha + (\beta+p\cdot\overline{\alpha-1})\, l_t^{\alpha-1} \tag{19}$$

This can be integrated to give

$$l_t^\alpha = \frac{l_o\, e^{-(\beta+p\alpha)t}}{\alpha!}\left(\frac{\beta}{p}\right)\left(1+\frac{\beta}{p}\right)\cdots\left(\alpha-1+\frac{\beta}{p}\right)(e^{pt}-1)^\alpha \tag{20}$$

with

$$\frac{d(\log \mu_t l_t)}{dt} = -(\beta+\overline{\alpha-1}\, p) + \frac{(\alpha-1)\, p\, e^{pt}}{e^{pt}-1} \tag{21}$$

Here again the form of equation (21) does not accord with observations from human data.

21. In the attempts to fit these forward type formulae to human data it was found (Beard, 1950, 1952*c*) that satisfactory numerical results could be obtained by expressing $\mu_t l_t$ in gamma function form subject to a terminal age ω, i.e. the infinite tail of the curve is the opposite way round to what would be considered natural. This formula, after elimination of a constant element representing accidental mortality, can be derived from the difference-differential equation

$$\frac{dl_t^\alpha}{dt} = pl_t^\alpha - p_t^{\alpha-1} \tag{22}$$

the solution of which leads to

$$l_t^{\alpha} = l_o\, e^{-p(\omega-t)}\, \{p(\omega-t)\}^{\alpha}/\alpha! \tag{23}$$

from which

$$\frac{d(\log \mu_t l_t)}{dt} = p - \frac{\alpha-1}{\omega-t}$$

if the deaths occur at the αth hit. In this formula $p \sim 0{\cdot}3$, $\alpha \sim 11$ and $\omega \sim 110$ for human mortality.

22. No obvious physical model applies to equation (22), but the relationship can be written in the backward form

$$\frac{dl_t^{\alpha}}{dt} = -\frac{\alpha}{\omega-t}\, l_t^{\alpha} + \frac{\alpha+1}{\omega-t}\, l_t^{\alpha+1} \tag{24}$$

in which the rate at which a unit is lost is proportional to the number of units remaining divided by the years of life remaining to the final age ω. From a biological point of view the concept of a final age by which the organism must be dead is unsatisfactory, but the fact that satisfactory numerical results arise only from a backward formula suggests that a closer study of this type of model might be more profitable.

23. The simplest backward model arises from the relationship

$$\frac{dl_t^{\alpha}}{dt} = -pl_t^{\alpha} + pl_t^{\alpha+1} \tag{25}$$

where the organism is assumed to lose a unit at rate p.
This has a solution

$$l_t^{\alpha} = l_o\, e^{-pt}\, (pt)^{n-\alpha}/(n-\alpha)! \tag{26}$$

where n is a maximum number of units. If death is assumed to occur when the number of units falls below r, we have

$$\frac{d(\log \mu_t l_t)}{dt} = -p + \frac{n-r}{t} \tag{27}$$

This is of similar form to equation (16) and is not suitable for human data.

24. By assuming that the rate of loss of a unit is proportional to the number of units remaining the relation

$$\frac{dl_t^{\alpha}}{dt} = -p(\beta+\alpha)\, l_t^{\alpha} + p(\beta+\alpha+1)\, l_t^{\alpha+1} \tag{28}$$

may be set up. This has the solution

$$l_t^{\alpha} = k\, e^{pt}/(1+D\, e^{pt})^{\beta+\alpha+1} \tag{29}$$

If death occurs when the units fall below α, we have

$$\begin{aligned} l_t &= \sum_{\alpha} l_t^{\alpha} = k/(1+De^{pt})^{\beta+\alpha} \\ &= l_o\, D(1+D)^{\beta+\alpha}/(1+De^{pt})^{\beta+\alpha} \end{aligned} \tag{30}$$

We also have

$$\frac{d(\log \mu_t l_t)}{dt} = p - \frac{(\beta+\alpha+1)\, pDe^{p}}{1+De^{pt}} \tag{31}$$

and

$$\mu_t = \frac{p(\beta+\alpha)De^{pt}}{1+De^{pt}} \tag{32}$$

We have now found a difference equation model which leads to a Perks (logistic) formula for μ_t. In formula (31) the upper limit of μ_t is $p(\beta+\alpha)$; $p \sim 0{\cdot}1$ and the limit $\sim 0{\cdot}7$ so that $(\beta+\alpha) \sim 7$.

25. The distribution of α in the population at age 0 implied by equation (29) is a decreasing geometrical progression, i.e.

$$\frac{D}{1+D}, \frac{D}{(1+D)^2}, \cdots \frac{D}{(1+D)^{\alpha}}$$

For human mortality D is small (of the order of 10^{-5}) so that the distribution is very slowly decreasing with increasing α.

26. The significant result which emerges from the experiments made along these lines is that to provide results which have some reasonable semblance to observed human mortality the backward type of model has to be adopted. This is consistent with death being regarded as the culmination of a degenerative process such that death occurs when the organism reaches a certain level of degeneration. The mathematical models are based on numerical results for adult ages and interpolation back to birth is possibly a questionable process, a more suitable approach being to regard the life and death process as a period during which the organism is building up to a complex situation with a subsequent degeneration. This would lead to models in which the whole of life process would be looked upon as the resultant effect of two opposing forces.

27. Calculation of the moments of the distribution of deaths by age for a population of mice (Greenwood, 1928) shows that a Pearson type III (gamma function) would give a fair representation, but, as with the human data, the curve is the "opposite way round", i.e. subject to a terminal age. By inference the Perks (logistic) curve would give a fair representation of this data. No calculations have been made on animal data or on physical objects such as electric light bulbs and motor cars (e.g. Cramer, 1958) but it would seem worth while trying to find out if observed data of this latter type would distinguish between the two types of processes.

REFERENCES

BEARD, R. E. (1936). *J. Inst. Actu.*, **67**, 53.
BEARD, R. E. (1939*a*). *J. Inst. Actu.*, **70**, 53.
BEARD, R. E. (1939*b*). *J. Inst. Actu.*, **70**, 373.
BEARD, R. E. (1950). *Proc. Centen. Assembl. Inst. Actu.*, **2**, 89.
BEARD, R. E. (1951*a*). *J. Inst. Actu.*, **77**, 382.
BEARD, R. E. (1951*b*). *J. Inst. Actu.*, **77**, 394.
BEARD, R. E. (1952*a*). *J. Inst. Actu.*, **78**, 82.
BEARD, R. E. (1952*b*). *J. Inst. Actu.*, **78**, 201.
BEARD, R. E. (1952*c*). *J. Inst. Actu.*, **78**, 341.
CRAMER, J. S. (1958). *J. R. statist. Soc.*, **121**, 18.
GOMPERTZ, B. (1825). *Phil. Trans.*, **115**, 513.
GREENWOOD, M. (1928). *J. Hyg.* (*Lond.*), **28**, 282.
MAKEHAM, W. M. (1867). *J. Inst. Actu.*, **13**, 325.
Mortality of Assured Lives (1956). *J. Inst. Actu.*, **82**, 3.
Papers of Royal Commission on Population (1950). **2**, 154.
PERKS, W. (1932). *J. Inst. Actu.*, **63**, 12.
PERKS, W. (1953). *J. Inst. Actu.*, **79**, 199.
Registrar General's Decennial Supplement, England and Wales 1951, Review in *J. Inst. Actu.*, **83**, 168 (1957).

AUTHOR INDEX

Plain numbers indicate a contribution either in the form of an article or as a contribution to the discussions. Italic numbers indicate a reference to an author's work.

SUBJECT INDEX

Printed by Spottiswoode, Ballantyne & Co. Ltd., London and Colchester

CUMULATIVE INDEXES TO VOLUMES 1–5

AUTHOR INDEX

Numbers in bold type indicate volume number. Plain numbers indicate a contribution either in the form of an article or as a contribution to the discussions. Italic numbers indicate a reference to an author's work.

SUBJECT INDEX

Figures in heavy type indicate volume number. Figures in ordinary type indicate page number.

Printed by Spottiswoode, Ballantyne & Co. Ltd., London and Colchester